COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

HEARING

BEFORE THE

SUBCOMMITTEE ON
INVESTIGATIONS AND OVERSIGHT

AND THE

SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT

AND THE

SUBCOMMITTEE ON
SCIENCE, RESEARCH AND TECHNOLOGY

OF THE

COMMITTEE ON
SCIENCE AND TECHNOLOGY
HOUSE OF REPRESENTATIVES

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CONTENTS

WITNESSES

July 23, 1986: Page

- Dr. David T. Kingsbury, Assistant Director, Biological, Behavioral, and Social Sciences, National Science Foundation 8
- Dr. Margaret Mellon, director, Toxic Substances Program, Environmental Law Institute 45
- Dr. Monica Riley, professor of biochemistry, State University of New York at Stony Brook, and American Society for Microbiology, and chairman, Committee on Genetic and Molecular Microbiology of the Public and Scientific Affairs Board 59
- Dr. Elliott A. Norse, director, Public Affairs Office, the Ecological Society of America 74
- Dr. John A. Moore, Assistant Administrator for Pesticides and Toxic Substances, U.S. Environmental Protection Agency 97
- Dr. Orville G. Bentley, Assistant Secretary for Science and Education, U.S. Department of Agriculture, accompanied by Karen Darling, Deputy Assistant Secretary for Marketing and Inspection Service 108
- Richard Godown, Industrial Biotechnology Association, accompanied by Dr. Alan Goldhammer 155

APPENDIXES

1. National Science Foundation followup questions and answers for the record 171
2. American Society for Microbiology followup questions and answers for the record 176
3. Environmental Law Institute followup questions and answers for the record 178
4. Ecological Society of America followup questions and answers for the record 181
5. U.S. Environmental Protection Agency followup questions and answers and edited oral remarks submitted for the record 184
6. U.S. Department of Agriculture followup questions and answers and edited oral remarks submitted for the record 211
7. National Institutes of Health, Recombinant DNA Advisory Committee, followup questions and answers for the record 248
8. Charter: Biotechnology Science Coordinating Committee of the Federal Coordinating Council for Science, Engineering, and Technology 252
9. NIH report of Committee—ACTION 256
10. Request for clarification by Margaret Mellon of ELI 282

COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY

WEDNESDAY, JULY 23, 1986

House of Representatives, Committee on Science and Technology, Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources, Agriculture Research and Environment, and the Subcommittee on Science, Research and Technology,

Washington, DC.

The subcommittees met, pursuant to notice, at 9:40 a.m., in room 2325, Rayburn House Office Building, Hon. James Scheuer presiding.

Mr. Scheuer. The Subcommittee on Natural Resources, Agriculture Research and Environment, the Subcommittee on Investigations and Oversight, and the Subcommittee on Science Research and Technology—three subcommittees of the Science and Technology Committee, who are conducting this hearing jointly—these subcommittees announce that this meeting is coming to order.

We have made some inquiry as to whether we couldn't move into the big hearing room, but with the cameras here and the mikes all in place, we will proceed here. The subcommittees will come to order for a hearing on the Federal Policy Statement for the Coordination of Biotechnology Regulation.

You may remember, some of you, that in early June the Natural Resources Subcommittee and the Science Research and Technology Subcommittee held joint hearings on H.R. 4452, the Biotechnology Science Coordination Act of 1986, and the subcommittees invited representatives of the OSTP, the science and technology policy group, and the various Federal agencies involved in the regulation of biotechnology products to discuss their views on the bill and the administration's plan for regulating biotechnology products.

The OSTP witnesses testified in opposition to the bill, stating that the administration's plan for regulating biotechnology was adequate and that the bill was unnecessary.

The OSTP witnesses, however, refused to discuss the details of the administration's biotechnology plan, since it hadn't been signed by the President at that time. Now that the regulations have been published, we are pleased that we will have the opportunity today to hear about how this policy was developed and how the various Federal agencies plan to implement the policy statement.

While the new guidelines raise a number of issues, I am going just to express one concern here. Despite more than 2 years of effort, the guidelines still fail to provide the kind of definitive final guidance that the biotechnology industry urgently needs. Critical questions remain unresolved.

For example, the question of what types of organisms will be subject to regulatory review is even now open for a 90-day public comment period. Major parts of the USDA, the Department of Agriculture, and the EPA regulatory scheme must be implemented by a rulemaking, a process that is likely to last for a year or more, and critical definitions are entirely lacking; for example, definitions of what constitutes "a release into the environment."

Industry needs certainty on these issues to understand what its obligations are. The public needs certainty on these issues to ensure that adequate environmental protections are in place. We do not want to see a repeat of last year's episode where researchers claimed that a tree and a pig were both "contained facilities" for the purpose of using genetically-altered organisms outside of laboratory confinement. Frankly, given the effect of these episodes on the industry's credibility and the public confidence, I suspect the industry would prefer not to see a repeat of these episodes either.

It appears to me that the Biotechnology Science and Coordinating Committee has shirked its responsibility for resolving these continuing uncertainties, and I hope very much that the witnesses today will address this concern as well as other issues which we have raised on prior occasions, and I am looking forward to their testimony.

First, without objection, we will place in the record at this point the opening statement of Congressman Manuel Lujan.

[The prepared opening statement of Mr. Lujan follows:]

OPENING STATEMENT
HON. MANUEL LUJAN, JR. (R-NM)
HEARING ON FEDERAL COORDINATING POLICY FOR BIOTECHNOLOGY
JULY 23, 1986

MR. CHAIRMAN:

TODAY'S HEARING IS INTENDED TO REVIEW THE FEDERAL REGISTER ANNOUNCEMENT OF JUNE 26, 1986, WITH REGARD TO THE "COORDINATED FRAMEWORK FOR REGULATION OF BIOTECHNOLOGY: ANNOUNCEMENT OF POLICY AND NOTICE FOR PUBLIC COMMENT."

THE ADMINISTRATION, THROUGH THE FEDERAL REGISTER ANNOUNCEMENT, HAS SOUGHT TO INITIATE A PROCESS WHEREBY THE HEALTH AND SAFETY OF THE PUBLIC AND OUR ENVIRONMENT CAN BE PROTECTED THROUGH FEDERAL REGULATIONS IN LIEU OF AN EMERGING NEW TECHNOLOGY, THAT IS, BIOTECHNOLOGY, WHICH HAS THE POTENTIAL FOR REVOLUTIONIZING THE MEDICAL, AGRICULTURAL, AND PHARMACEUTICAL FIELDS.

A 1984 NATIONAL ACADEMY OF SCIENCE REPORT ESTIMATED THE POTENTIAL FOR THIS MARKET TO BE IN THE TENS OF BILLIONS OF DOLLARS. AND, SINCE 1976, MORE THAN 200 NEW BUSINESSES HAVE FORMED IN THE U.S. TO TAKE ADVANTAGE OF BIOTECHNOLOGY TECHNIQUES. THIS NEW INDUSTRY HAS ALREADY CREATED 5,000-10,000 NEW JOBS IN THE UNITED STATES ALONE. IT IS CLEAR THAT WITH THE EMERGENCE OF SUCH A PROMISING INDUSTRY, BALANCE MUST BE ATTAINED WITH

ENVIRONMENTAL AND PUBLIC HEALTH AND SAFETY CONCERNS.

I WOULD REMIND THE COMMITTEE OF THE UNFORTUNATE SITUATION CONGRESS AND THE NATION FOUND THEMSELVES IN DURING THE LATE 60S AND THROUGH THE 1970S. THIS NATION FAILED TO ANTICIPATE THE NEGATIVE CONSEQUENCES OF THE PETROCHEMICAL AND PESTICIDE INDUSTRIES AND THEREFORE HAD TO RESPOND AFTER THE FACT -- AND IN A "CRISIS SYNDROME" -- THERBY MAKING LEGISLATION OF ULTIMATE NECESSITY.

THE APPROACH TAKEN BY THE ADMINISTRATION IS A CONTRAST TO "CRISIS MANAGEMENT." PUBLICATION OF A FEDERAL FRAMEWORK FOR REGULATING BIOTECHNOLOGY IS A "PROGRESSIVE" APPROACH. AND I MIGHT ADD, THE LENGTH OF TIME IT HAS TAKEN THE FEDERAL AGENCIES TO CULMINATE THIS ACTIVITY HAS FAR EXCEEDED, IN GENERAL, PAST PERFORMANCE BY THE FEDERAL BUREAUCRACY. EVEN REAUTHORIZATION OF VERY IMPORTANT ENVIRONMENTAL LEGISLATION HAS TAKEN CONGRESS YEARS TO ACHIEVE.

HOWEVER, IN BEING "PROGRESSIVE" RATHER THAN REACTIVE, THESE REGULATIONS WILL BE SUBJECT TO FAR MORE SCRUTINY THAN PERHAPS THE REACTIVE APPROACH DRAWS. IT IS THE ROLE OF THIS COMMITTEE TO ASSURE AN OPEN, FAIR, BALANCED AND COMPREHENSIVE REVIEW.

WE LOOK TO THE WITNESSES TODAY TO NOT ONLY AID THE COMMITTEE IN CLARIFYING ASPECTS OF AND IDENTIFYING CONCERNS REGARDING THE REGULATIONS, BUT TO ALSO MAKE CONSTRUCTIVE AND SOUND

RECOMMENDATIONS. IF THERE ARE PERCEIVED FLAWS, WE WANT TO HEAR THAT, AND ALSO HEAR CREDIBLE WAYS TO CORRECT THEM. WE WANT TO HEAR OF THE POSITIVE AND SOLID ASPECTS OF THIS FRAMEWORK AND HOW YOU PERCEIVE ITS OPERATION.

I AM PLEASED THAT THE SUBCOMMITTEE ACCEPTED THE RECOMMENDATION OF THE MINORITY TO INVITE A WITNESS FROM THE ECOLOGICAL COMMUNITY. WE ARE PLEASED TO HAVE THE ECOLOGICAL SOCIETY OF AMERICA PRESENT TO AID IN OUR BALANCED APPROACH.

WE THANK ALL THE WITNESSES FOR THEIR THOUGHTFUL AND DILIGENT RESPONSE TO TESTIFY.

THANK YOU.

Mr. **Scheuer**. Now let us hear any statements from my colleagues. The ranking minority member of our subcommittee, Hon. Claudine Schneider of the State of Rhode Island.

Miss **Schneider**. Thank you, Mr. Chairman. I look forward to the testimony we will be hearing this morning. I think that when we discuss biotechnology regulations, it revolves around how one views the biotechnology products, and in that regard I think that the regulations that we will be discussing in some detail is a positive step in the right direction. There is very little question that we have to use a balanced approach, in that we have the opportunity to utilize biotechnology as one of our most competitive edges in terms of balancing our imbalance of trade at this time. In 1984 the National Academy of Sciences had done a study which estimated that between $40 billion and $100 billion a year potential lies in the biogenetic engineering technology.

There is very little question in my mind that any regulatory scheme must be designed to provide industry with clear and certain regulatory direction; secondly, to prevent the introduction of harmful biotechnological products; and third, to build and maintain public confidence.

Needless to say, those three challenges are monumental. They may sound slight, but achieving that balance is what our goal is here today, and also in devising the appropriate regulatory approach. I am concerned that some of the regulatory decisions, particularly at the Department of Agriculture may lack the necessary rigor, and I will be looking forward to an in-depth discussion of particularly what the Department of Agriculture is going to be proposing.

There is no question that there are gaps in our knowledge and that those gaps need to be addressed, but I feel that it is imperative that we address two specific things: that we give citizens the opportunity to participate in the review and decisionmaking process; and secondly, that we make sure that we are not creating impediments to business to pursue the kind of activities that I think our country can continue to provide the lead in worldwide.

Thank you, Mr. Chairman.

Mr. **Scheuer**. Thank you very much.

Now, Congressman Harold Volkmer of Missouri, who is chairman of the Investigations and Oversight Subcommittee, which is cochairing these hearings—and incidentally, Congressman Volkmer will be chairing this afternoon's session.

Congressman Volkmer.

Mr. **Volkmer**. Thank you very much, Chairman Scheuer. I welcome the opportunity to join with the Subcommittee on Science Research and Technology and, the Natural Resources, Agriculture Research and Environment Subcommittee, to examine the administration's proposed coordinated framework for regulation of biotechnology.

Now, the proposed guidelines represent the third stage in the history of biotechnology regulation. The first stage focused on laboratory research in genetic engineering, and the National Institutes of Health, which through its Recombinant DNA Advisory Committee, provided the guidelines for such research. These guidelines were exceptionally successful in balancing progress with caution.

They continue to provide the model of biotechnology research guidelines around the world.

The second stage of biotechnology development began on December 31, 1984, with the publication of the Federal agencies' interim guidelines for the regulation of biotechnology. These guidelines were intended to provide the regulatory safeguards applicable to the first deliberate releases of genetically engineered organisms. In December 1985 the Investigations and Oversight Subcommittee held a hearing in this room to review the implementation of these guidelines.

While the agencies' testimony was encouraging, events occurring outside the hearing room were not. Through subsequent investigation, this subcommittee learned of unauthorized rooftop experiments with the so-called ice-minus bacteria, as well as unauthorized testing of a genetically-engineered animal vaccine by scientists in Texas.

Coincidental with these unauthorized releases, many companies who were trying to play by the regulatory rules were losing hope they would ever learn what the rules were. Proposals for environmental releases were bounced from one agency to another or were allowed to languish within an agency. More often than not, this delay was not due to scientific caution, but due to regulatory confusion and paralysis.

The second stage of biotechnology has not been encouraging. The unauthorized releases and the regulatory confusion have eroded, for the time being, the public's confidence in both industry and the Government's ability to chart a safe course for biotechnology.

Now, with the publication of the administration's proposed framework, we enter the third stage of biotechnology development with the hope that biotechnology can reclaim the high ground of public confidence and scientific progress. We are here today to inquire whether these guidelines provide the caution and clarity necessary to fulfill that hope. Biotechnology should and must be developed for the benefit of mankind. For this to happen, we need more than scientific progress and new guidelines. We will need the increased vigilance of Federal agencies, candor and caution by the biotechnology industry, and the enlightened participation of the public in the difficult decisions ahead.

I look forward to the testimony of our witnesses today, and yield back the balance of my time to the Chair.

Mr. **Scheuer**. Thank you.

Congressman Ron Packard of California, who is the ranking Republican on the Investigations and Oversight Subcommittee.

Mr. **Packard**. Thank you, Mr. Chairman. I am very pleased this morning to have before me the final coordinated framework for regulation of biotechnology. I know the Office of Science and Technology Policy and the various agencies have been working diligently on these guidelines for some time, and I feel on the whole, they have done a good job.

While there are still portions of the guidelines that raise legitimate questions, I believe that putting these guidelines into place is a positive and responsible action on the part of the Federal Government. They will undoubtedly have to be fine-tuned as the biotechnology industry matures and as our research base expands. However, these guidelines form the foundation needed to ensure the safety of health and the environment as biotechnology research and product development continues.

I am pleased that the subcommittee has called this hearing. I am hopeful that our discussion today will contribute to a better understanding of the Federal guidelines and their implementation.

Thank you, Mr. Chairman, for the opportunity to join with you in this hearing.

Mr. **Scheuer**. I am going to ask unanimous consent to leave the record open for further opening statements by members of the three subcommittees who may come in at a later point. Hearing no objection, so ordered.

All right, we will now hear from Dr. David Kingsbury, Chairman of the Biotechnology Science Coordinating Committee.

Dr. Kingsbury, why don't you take perhaps 8 or 10 minutes to sum up, preferably not reading your testimony, but speaking to us informally, and then I am sure we will have some questions for you.

STATEMENT OF DR. DAVID T. KINGSBURY, ASSISTANT DIRECTOR, BIOLOGICAL, BEHAVIORAL, AND SOCIAL SCIENCES NATIONAL SCIENCE FOUNDATION

Dr. **Kingsbury**. Sir, I would like to summarize certain portions of the testimony. Mr. Chairman, members, and staffs of the subcommittees, as you know, I am David T. Kingsbury, Assistant Director for Biological, Behavioral, and Social Sciences, National Science Foundation.

As you have requested, I am here today to provide the subcommittees with an overview of the administration's policy for the regulation of biotechnology research and products. The following explanation is given from my perspective based on my service on the Domestic Policy Council Working Group on Biotechnology and the Biotechnology Science Coordinating Committee, the so-called BSCC, of the Federal Coordinating Council on Science, Engineering and Technology.

The first part of the administration's two-part policy appeared in the November 14, 1985, Federal Register and announced the establishment of the BSCC. The BSCC consists of: the Commissioner of the Food and Drug Administration; the Director of the National Institutes of Health; the Assistant Secretary for Agriculture for Marketing and Inspection Services; the Assistant Secretary of Agriculture for Science and Education; the Assistant Administrator of EPA for Pesticides and Toxic Substances; the Assistant Administrator of EPA for Research and Development; and myself. The committee operates under guidance from its charter and a memorandum of understanding signed by each of the members.

The second part of the policy was published June 26, 1986, and consists of six elements: the preamble; and statements of policy from the Food and Drug Administration; the Environmental Protection Agency; the U.S. Department of Agriculture; the Occupational Safety and Health Administration; and, the National Institutes of Health.

The Federal Register policy statement seeks to show how the separate agencies' policies form a coordinated framework. Each of the agencies' statements stands alone. Each describes the agencies' separate and respective policies. The preamble is essentially an executive summary, providing an overview of what is biotechnology, what are the agencies' separate policies, and how they work together. Charts I and II, for example, summarize the agencies' respective responsibilities for biotechnology products or research.

There are many elements to the coordination of Government regulatory policy in any area of regulation, and this is especially true for biotechnology. Biotechnology encompasses processes as different as farming, the production of enzymes for laundry detergents, and the genetic-engineering of bacteria to clean up oil spills or to produce interferon or growth hormones.

Biotechnology includes myriad dissimilar processes, producing even more disparate products for vastly different applications. Biotechnology is not a single entity, but is in fact a broadly applicable enabling technology.

Government regulation is not organized around technological processes, but rather tends to be structured around products developed by various technologies for specific intended purposes. Therefore, one critical element in the coordinated regulatory framework is the common definition of the nature of the product subject to particular types of regulatory oversight.

The issue of definitions came before the BSCC as the members represented the particular agencies developing them. The BSCC felt that uniformity across agencies, to the extent possible and appropriate, would strengthen and simplify the regulatory structure. Uniformity would also tend to discourage "agency-shopping" by the regulated community seeking to find a sympathetic regulatory agency.

It would be appropriate to review briefly each part of the recent notice. The preamble, as I mentioned earlier, is essentially the executive summary of the full policy. The agencies' statements represent the refinement of the proposed policies published in December 1984 and therefore are final. Part of EPA's policy are implemented immediately; other aspects require rulemaking. Similarly, the USDA policy requires some rulemaking for implementation and proposed rules are included in this publication.

The EPA and USDA have requested voluntary compliance with their policy prior to publication of the final rules.

Questions have arisen regarding those Government agencies which fund research related to biotechnology, but did not publish policies in this notice. Those agency policies were referenced in chart II of the preamble, but were not explained in detail.

All Federal agencies that fund research related to biotechnology adhere to the policy that this research must conform to the requirements of the coordinated framework, such as the National Institutes of Health Recombinant DNA guidelines. Each agency will use one of the three research review committees—NIH, NSF, or USDA—that would be the most appropriate, and then will provide that committee with the necessary materials for review. The review committee, of course, will be free to deal directly with the investigator if additional documentation is needed.

A principal focus of the new policy is environmental release of new organisms. There has been general acceptance of the regulation of nonliving products of biotechnology and, in fact, the new policy reiterates that such regulatory practices will be maintained.

Of equal significance to the current policy is the future implementation of the policy and the continued coordination of agency activity. While it is clearly the statutory responsibility of each agency to carry out its function, it is also the role of the BSCC to help in the coordination and development of full implementation.

The BSCC has planned a full and active course for the future. The committee will carry out the majority of its work through a subcommittee structure designed to provide a broad multiagency and, in some cases, nongovernmental representation and public participation.

At present, the BSCC has established five subcommittees: subcommittee on risk assessment; a subcommittee on greenhouse containment standards and definitions of "containment" and "release;" subcommittee on training; subcommittee on research and research needs; and subcommittee on public information and education.

I would like to describe the operation of the greenhouse subcommittee as a means of describing future operations. This subcommittee has been established under the joint leadership of Dr. Moore of EPA and Dr. Bentley of USDA, and a clear plan of operation has been established. Their group will number between 9 and 11 people drawn from Government, universities, and private industry. Their charge is to develop comprehensive standards for the design and operation of greenhouses for contained experimentation. In the process of their work, they are also responsible for developing appropriate definitions for containment and release.

The subcommittee is due to report to the BSCC in early 1987. The subcommittee has been encouraged to operate as openly as possible and to use a broad range of expertise. The cochairmen will report the groups' findings back to the BSCC. Adoption of the final report for publication in the Federal Register will occur at a subsequent meeting of the BSCC. The recommendations will be published for public comment, and those comments will be reviewed prior to publishing in final.

We expect that this whole process will be completed approximately one year from now.

The BSCC will continue to have the primary responsibility for the scientific questions that arise in the future, including questions associated with risk assessment methodology and its further development and implementation. The BSCC will not be involved with questions regarding risk management and other agency-specific policy issues. These are management questions well outside the purview of the BSCC and that more properly fall to the agency heads and administration policy makers.

However, we expect to be able to fulfill our charter and extend agency coordination into questions of data submission requirements. In a fast-moving technological environment, it is necessary to regularly review the appropriateness of the scientific basis of existing legislation—regulation. I am sorry. The BSCC considers this its major responsibility, including recommendations to modify existing statutes, if it is deemed necessary. At present, however, we are very confident that the existing regulation covers the current and near-term biotechnology industry.

Since the release of the policy, we have endeavored to provide for broad public discussion. Following the approval of the policy, we held a general open briefing at the National Science Foundation. This briefing was well attended by members of the press, congressional staff, public interest groups, and representatives of industry. Subsequently, some of the individual agencies held specific detailed briefings as well.

Following publication on June 26, we held a special briefing at the State Department for the international community, and it too was very well attended.

On July 9, 1986, the BSCC held its first open public meeting. The meeting was attended by approximately 80 people and provided the public with information about BSCC operations and an overview of the policy statement. The public was invited to participate in the meeting, and it ended with an open question-and-answer session.

It is our intention to continue this essential open public discussion. To the extent possible, we will maintain an open process during any legal challenge aimed at preventing implementation of the coordinated framework.

Thank you for the opportunity to appear at this joint subcommittee hearing. I would be pleased to answer any questions you might have.

[The prepared statement of Dr. Kingsbury follows:]

National
Science
Foundation

STATEMENT OF

DR. DAVID T. KINGSBURY

ASSISTANT DIRECTOR
BIOLOGICAL, BEHAVIORAL, AND SOCIAL SCIENCES
NATIONAL SCIENCE FOUNDATION

BEFORE THE

HOUSE COMMITTEE ON SCIENCE AND TECHNOLOGY

U.S. HOUSE OF REPRESENTATIVES

JULY 23, 1986

Mr. Chairmen, Members, and Staffs of the Subcommittees:

I am David T. Kingsbury, the Assistant Director for Biological, Behavioral, and Social Sciences of the National Science Foundation. As you requested, I am here today to provide the subcommittees with an overview of the Administration's policy for the regulation of biotechnology research and products. The following explanation is given from my perspective based on my service on the Domestic Policy Council Working Group on Biotechnology, and the Biotechnology Science Coordinating Committee (BSCC) of the Federal Coordinating Council on Science, Engineering and Technology (FCCSET).

The first part of the Administration's two part policy appeared in the November 14, 1985 Federal Register and announced the establishment of the BSCC. The BSCC consists of the Commissioner of the Food and Drug Administration, the Director of the National Institutes of Health, the Assistant Secretary of Agriculture for Marketing and Inspection Services, the Assistant Secretary of Agriculture for Science and Education, the Assistant Administrator of EPA for Pesticides and Toxic Substances, the Assistant Administrator of EPA for Research and Development, and myself. The Committee operates under guidance from its charter and a Memorandum of Understanding signed by each of the members. We have established the rule that the committee consists of principals only and no member is allowed to send a representative in his place. The Committee has met approximately monthly since its establishment and its initial activities included the consideration of scientific issues which arose during the development of the Administration's Coordinated Regulatory Framework.

The second part of the policy was published June 26, 1986 and consists of six elements, the preamble and statements of policy from the Food and Drug Administration, the Environmental Protection Agency, The U.S. Department of Agriculture, the Occupational Safety and Health Administration and the National Institutes of Health. Also published at the same time were proposed U.S. Department of Agriculture rules governing the Introduction of Organisms and Products Produced through Genetic Engineering which are Plant Pests and an Advanced Notice of Proposed Guidelines for Biotechnology Research, also from USDA.

The Federal Register policy statement seeks to show how the separate agencies' policies form a coordinated framework. Each of the agency statements stands alone; each describes the agency's separate and respective policy. The preamble is essentially an executive summary, providing an overview of what is biotechnology, what are the agencies' separate policies, and how they work together. Charts I and II, for example, summarize the agencies' respective responsibilities for biotechnology products or research.

The preamble also describes the BSCC efforts to coordinate scientific aspects of agency activities in biotechnology. One effort was to coordinate, as appropriate, the definitions of the items to be regulated, used by each of the agencies. I will discuss the definitions further in a moment. The BSCC section also mentions concern regarding "release", and requests comments on ways to define it. In addition, the preamble mentions international policy and expresses the OECD principles relating to recombinant DNA safety and regulation.

There are many elements to the coordination of government regulatory policy in any area of regulation and this is especially true for biotechnology. Remember that biotechnology is the application of biological systems and organisms to any technological or industrial process. It encompasses processes as different as farming, the production of enzymes for laundry detergents, and the genetic engineering of bacteria to clean up oil spills or to produce interferon or growth hormone. Biotechnology includes myriad dissimilar processes producing even more disparate products for vastly different applications. Biotechnology is not a single entity, but is, in fact, a broadly applicable enabling technology.

Government regulation is not organized around technological processes, but rather tends to be structured around products, developed by various technologies for specific intended purposes. Therefore, one critical element in a coordinated regulatory framework is the common definition of the nature of the products subject to particular types of regulatory oversight.

In the December 1984 Federal Register Notice, which outlined the proposed coordinated framework, EPA proposed a definition of a "new" organism to be regulated under the Toxic Substance Control Act, commonly called TSCA. The proposed definition was "process" based. A microorganism would be considered "new" if significant human intervention had been used to develop it. Microorganisms developed by recombinant DNA and cell fusion techniques were presumed to be new because they involved significant human intervention.

There were many comments to the EPA definition. Subsequent consideration of the comments was fully described in the EPA section of the June 26 notice.

While EPA was developing the definitions of intergeneric organism and pathogen, USDA's Animal and Plant Health Inspection Service (APHIS) was also reviewing the comments it received from its December 1984 Federal Register Notice. APHIS and USDA's researchers under the Assistant Secretary for Science and Education were seeking to define those categories of products or research that should be subject to USDA review. USDA staff were benefitting from their own expert analysis and the approaches being developed by EPA.

The issue of definitions came before the BSCC as the members represented the particular agencies developing them. The BSCC felt that uniformity across agencies, to the extent possible and appropriate, would strengthen and simplify the regulatory structure. Uniformity would also tend to discourage "agency shopping" by the regulated community seeking to find a sympathetic regulatory agency.

The BSCC in its role as a science coordinating body recognized that EPA's definitions would take effect immediately upon publication of the Federal Register Notice as it would be EPA's final notice. This immediate effect was important to insure that "new" microorganisms would become subject to review on the date of the notice. The BSCC believed it would be useful to specifically solicit the views of the public, and thus, has asked for comments. Comments received will be reviewed by the BSCC, and the BSCC will then consider what further steps, if any, should be taken to refine the BSCC definitions. It will be up to each agency itself to make any modifications to its own definitions. The BSCC will continue to work to promote consistency and coordination.

At this point I would like to apologize for an omission in the June 26, 1986 notice that may have caused some confusion. The signature block at the close of each agency's policy statement was inadvertently omitted. A correction was printed in the July 14, 1986 Federal Register. It should now be clear that the statement of each agency represents its respective policy.

It is appropriate to review briefly each part of the recent notice. The Preamble, as I mentioned earlier, is essentially the executive summary of the full policy. The agency statements represent the refinement of the proposed policies published in December 1984 and, therefore, are final. Parts of EPA's policy are implemented immediately, other aspects require rule making. Similarly, the USDA policy requires some rulemaking for implementation and proposed rules were included in this publication as I mentioned earlier. The EPA and USDA have requested voluntary compliance with their policy prior to publication of the final rules. The USDA has scheduled several public meetings, in California, Missouri and here in Washington, to collect public comments on their proposals relating to regulation and research.

Questions have arisen regarding those government agencies which fund research related to biotechnology but did not publish policies in this notice. Those agency policies were referenced in Chart II of the Preamble but were not explained in detail. All federal agencies that fund research related to biotechnology adhere to the policy that this research must conform to the requirements of the Coordinated Framework such as the National Institutes of Health Recombinant DNA Guidelines. Each agency will use one of the three research review committees, NIH, NSF or USDA that would be the most appropriate, and will then provide that committee with the necessary materials for review. The review committee, of course, will be free to deal directly with the investigator if additional documentation is needed. This mechanism will allow for the selection of the review committee with the most expertise in the given area required by the specific application and will ensure the highest quality of review.

A principal focus of the new policy is environmental release of new organisms. There has been general acceptance of the regulation of non-living products of biotechnology and, in fact, the new policy reiterates that such regulatory practices will be maintained. The new policy explains the application of certain statutes over genetically modified organisms, and in some cases imposes an abbreviated review over unmodified organisms when applied to environmental uses. There is a clear policy established requiring review of genetically engineered microorganisms prior to release in the environment with some organisms subject to an abbreviated review. For reference I refer you to the Summary Table in the EPA policy section (FR 51, No. 123, page 23319). This policy is now in effect, however, additional rule making is needed for full implementation of the policy. Until the rules are final, EPA expects persons introducing such organisms into the environment for non-agricultural uses to report to EPA voluntarily. In the unlikely event of a problem arising in this period of time EPA could use its authority under section 7 of TSCA to immediately limit or prohibit the manufacture, processing, distribution or use of the product. In addition USDA will review certain genetically engineered plant pests and animal pathogens.

Of equal significance to the current policy is the future implementation of the policy and the continued coordination of agency activity. While it is clearly the statutory responsibility of each agency to carry out its function, it is also the role of the BSCC to help in the coordination and development of full implementation. The BSCC has planned a full and active course for the future. The Committee will carry out the majority of its work through a subcommittee structure designed to provide a broad multi-agency and, in some cases, non-governmental representation and public participation. At present the BSCC has established the following subcommittees:

1. Subcommittee on risk assessment;
2. Subcommittee on greenhouse containment standards and definitions of "containment" and "release";
3. Subcommittee on training;
4. Subcommittee on research and research needs; and
5. Subcommittee on public information and education.

I would like to describe the operation of the greenhouse subcommittee as a means of describing future operations. This subcommittee has been established under the joint leadership of Dr. Moore of EPA and Dr. Bentley of USDA, and a clear plan of operation has been established. Their group will number between 9 and 11 people, drawn from government, universities and private industry. Their charge is to develop comprehensive standards for the design and operation of greenhouses for "contained" experimentation. In the process of their work they are also responsible for developing appropriate definitions for "containment" and "release." The subcommittee is due to report to the BSCC in early 1987. The subcommittee has been encouraged to operate as openly as possible and to use a broad range of expertise. The cochairmen will report the groups findings back to the BSCC. Adoption of the final report for publication in the Federal Register will occur at a subsequent public meeting of the BSCC. The recommendations will be published for public comment and those comments will be reviewed prior to publishing in final. We expect that this whole process will be completed approximately one year from now.

This process typifies what we believe will be the general model for BSCC operations. We will continue our present policy of "principals only" meetings at approximately monthly intervals and will supplement them with periodic open public meetings as deemed necessary or appropriate depending upon the issues before the Committee.

The current subcommittee structure is by no means final. Already, good suggestions for additional groups have been brought to our attention and will be seriously examined.

The BSCC will continue to have the primary responsibility for the scientific questions that arise in the future, including questions associated with risk assessment methodology and its further development and implementation. The BSCC will not be involved with questions regarding risk management and other agency specific policy issues. These are management questions well outside of the purview of the BSCC, and that more properly fall to the agency heads and Administration policy makers.

We do anticipate dealing with questions of agency jurisdiction for scientific review and the appropriate form of agency cooperation in the review process. When there are questions regarding the appropriate agency to review an application producers have been encouraged to contact the BSCC for clarification. We expect to be able to fulfill our charter and extend agency coordination into questions of data submission requirements as well.

In a fast moving technological environment it is necessary to regularly review the appropriateness of the scientific basis of existing regulation. The BSCC considers this its major responsibility, including recommendations to modify existing statutes if it is deemed necessary. For example, under the current policy certain classes of non-pathogenic microorganisms such as deletions or intrageneric constructions are subject to an abbreviated review because it is widely felt that they do not pose a threat to the environment. Moreover, as a practical matter there are no known products that fall into this classification. If any organisms appear to present additional concerns, then the BSCC feels obligated to reexamine the question and if necessary recommend appropriate action that may include legislative correction. At present we are very confident that the existing regulation covers the current and near term biotechnology industry. As the technology changes we will continue to monitor the changes and the adequacy of the regulatory structure within the context of these new developments. The DPC Working Group and the BSCC both view the Coordinated Framework as an evolutionary document, rather than one which is static long into the future.

Since the release of the policy we have endeavored to provide for broad public discussion. Following the approval of the policy, we held a general open briefing at the National Science Foundation. This briefing was well attended by members of the press, congressional staff, public interest groups and representatives of industry. Subsequently, some of the individual agencies held specific detailed briefings as well. Following publication on June 26 we held a special briefing at the State Department for the international community and it was very well attended. This session not only gave the members of the international community an overview of the policy and the scientific basis for the policy but was followed by an open question and answer session.

On July 9, 1986 the BSCC held its first open public meeting. The meeting was attended by approximately 80 people and provided the public with information about BSCC operations and an overview of the policy statement. The public was invited to participate in the meeting and it ended with an open question and answer session. It is our intention to continue this essential, open public discussion. To the extent possible we will maintain an open process during any legal challenge aimed at preventing implementation of the Coordinated Framework.

Thank you for the opportunity to appear at this joint subcommittee hearing. I would be pleased to answer any questions you may have.

Mr. **Scheuer**. Thank you. We have been joined by Congressman Doug Walgren, who is chairman of the Science Research and Technology Subcommittee of the committee, one of the three sponsoring subcommittees.

We would be happy to hear from you, Doug, at this point.

Mr. **Walgren**. Well, thank you, Mr. Chairman, and I have an opening statement that I would like to submit for the record. I appreciate the interest that the other subcommittees have brought to this and the chance to join you today. Thank you.

[The prepared opening statement of Mr. Walgren follows:]

OPENING STATEMENT BY THE
HON. DOUG WALGREN

JOINT HEARING ON FEDERAL COORDINATION POLICY FOR BIOTECHNOLOGY

JULY 23, 1986

TODAY WE ADDRESS ONE OF THE MOST IMPORTANT TOPICS OF THE YEAR AS WE DISCUSS HOW TO SET UP AN APPROPRIATE REGULATORY SYSTEM FOR THE EMERGING BIOTECHNOLOGY INDUSTRY. BIOTECHNOLOGY VERY CLEARLY IS ONE OF THE MOST PROMISING SCIENTIFIC ACHIEVEMENTS OF THE CENTURY. THERE IS NO DOUBT THAT MAJOR PORTIONS OF THE WORLD ECONOMY WILL BE REVOLUTIONIZED BY IT. STARVING PEOPLES WILL BE FED THROUGH BIOTECHNOLOGICAL ACHIEVEMENTS. MAJOR ENVIRONMENTAL PROBLEMS WILL BE NEUTRALIZED WHILE HUMAN AND ANIMAL DISEASES WILL BE CONQUERED. THIS GROUP OF TECHNOLOGIES PERHAPS MORE THAN ANY OTHER WILL INCREASE HUMAN CONTROL OVER THE FORCES OF NATURE.

THE ECONOMIC STAKES OF BIOTECHNOLOGY ARE GREAT AND RELATED PRESSURES WILL BE GREAT. THE AREAS OF THE COUNTRY AND THE WORLD THAT TAKE THE LEAD IN BIOTECHNOLOGY ALMOST CERTAINLY WILL PROSPER. THERE ARE ALREADY COMPANIES SPRINGING UP IN THE PITTSBURGH AREA AND MANY OTHER PARTS OF THE COUNTRY WHICH HAVE THE POTENTIAL TO TRANSFORM THIS NASCENT INDUSTRY INTO ONE OF THIS COUNTRY'S BIGGEST BY THE TURN OF THE CENTURY IF NOT SOONER. COMPETITION OVERSEAS IS ALREADY FORMIDABLE SO WE CANNOT AFFORD TO DELAY THESE COMPANIES WITH UNNECESSARY RED TAPE WHICH CAUSES THIS IMPORTANT INDUSTRY TO DEVELOP OVERSEAS.

HOWEVER, WE HAVE LEARNED THE HARD WAY THAT REVOLUTIONARY TECHNOLOGICAL ADVANCEMENT, ESPECIALLY WHEN IT ALTERS THE ENVIRONMENT, MUST BE APPROACHED VERY CAREFULLY. WE HAVE SEEN TOO MANY NEW

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TECHNOLOGIES OVERSOLD IN THE PAST TO BELIEVE THAT BIOTECHNOLOGY WILL BE WITHOUT ITS PITFALLS. THEREFORE, THE PUBLIC IS RIGHT IN DEMANDING THTA WE PROCEED WITH CAUTION AND SET STRICT GUIDELINES FOR THE UNLOCKING OF THE SECRETS OF THESE PROMISING NEW TECHNOLOGIES. IT IS NOT SURPRISING THAT IT HAS TAKEN THE BEST TALENT IN THE ADMINISTRATION MANY MONTHS TO COME UP WITH ITS PROPOSED SYSTEM OF REGULATION FOR BIOTECHNOLOGY AND I APPRECIATE THE CARE AND HIGH DEGREE OF CAUTION WITH WHICH THEY HAVE APPROACHED THE SUBJECT.

THEREFORE, THE TASK WE ARE FACING TODAY OF RESPONDING TO THESE REGULATIONS IS NOT EASY AND SHOULD NOT BE TAKEN LIGHTLY. YET GIVEN THE IMPORTANCE OF GETTING THIS INDUSTRY OFF TO A PROPER START, I AM HAPPY WE ARE UNDERTAKING IT.

Mr. SCHEUER. Very good. Thank you.

All right. We have been joined also by Jan Meyers of Kansas. Jan, do you have any opening statement?

Mrs. MEYERS. No. Thank you, Mr. Chairman.

Mr. SCHEUER. All right, then we will start with the questioning, and I will be happy to recognize Congresswoman Claudine Schneider of Rhode Island.

Miss SCHNEIDER. Dr. Kingsbury, Drs. Riley and Norse are later on going to be testifying that the BSCC's decision not to require strict review of certain types of genetically-engineered organisms prior to their release is not scientifically justified, and I know that you have been involved in that debate, so I would like to start off by hearing your response. There is quite a scientific dispute going on, as you know.

Dr. KINGSBURY. Well, I think that the—it's not a question of lack of review, the question is the level of review that's associated with a particular class of organisms.

If one refers to the EPA policy in the Federal Register, they have a summary table that describes prior notification and review of microorganisms applied to the environment, and within that, in their summary table which is an overview of their—of their policy, one finds that virtually every class of organisms is covered by one review policy or another and that the difference is not lack of review, but is an abbreviated review versus a full review. And so the question is one that revolves around the judgment of the scientific community and the scientists that were involved in helping EPA with their statement as to what constitutes an organism that should be subject to abbreviated review.

Miss SCHNEIDER. One of the things that I am concerned about in terms of an abbreviated review is the position that the Department of Agriculture seems to be taking in indicating that they don't feel that biotechnology products are really fundamentally different from many conventional products. That kind of thinking should lead us where?

Dr. KINGSBURY. Let me—let me go back and comment about different classes of biotechnology products. I think it's appropriate to put into perspective the kinds of questions we're asking here. As I pointed out in the testimony, biotechnology is not a unitary entity but is, in fact, an enabling technology. That enabling technology allows one to manipulate a variety of organisms, be they animals, plants, microbes, or viruses. Whatever the living entity is, it can be manipulated via the techniques that we're calling biotechnology or the enabling technology.

The kinds of questions that arise in different classes of biological organisms are really quite different. The notion that a genetically-engineered plant is significantly different because of the procedure used to produce that plant is different than the classic kinds of hybrid formation that has gone on does seem to be—is a position where it's unlikely that that plant would be dramatically different than one that could be derived by other mechanisms.

So I think that when the Agriculture Department makes the statement that they view this technology as not being radically different than the old ways, they're thinking in the context of—of—excuse me, of organisms with very large genomes in which we're doing very small manipulations and it's really more directed forms of producing new plant varieties. Under those conditions, their existing regulatory review of a new plant variety is rather stringent.

When one thinks of microorganisms—the're—we're looking at certainly more dramatic changes. All microorganisms that have been engineered, manipulated, would fall under regulation by the Environmental Protection Agency, so that there would be a review of microorganisms regardless of their application if they were engineered—manipulated. So I think we're really looking at two different kinds of approaches, but to two dramatically different classes of biological agents: higher organisms in terms of plants and animals in which the changes are not as likely to be as dramatic as they might be in a microorganism. It's really microorganisms that most of the policy focus is on.

Miss SCHNEIDER. Are you developing some kind of a Federal plan that will design how we are going to go about assessing the research on the effects of releasing genetically-engineered organisms into the environment, sort of like what we're doing on acid rain or on ocean pollution research?

Dr. KINGSBURY. The BSCC, as I mentioned, has a subcommittee on research and research needs, and part of the responsibility of that subcommittee is to review, together with the agencies. And this is a subcommittee now in which we have participation—or it's structured to have. It has not actually had its first meeting. We've had suggested memberships that would represent the research agencies and would allow them to coordinate among themselves in order to have a balanced approach to the research questions related to environmental release and the ecology of microorganisms.

The agencies obviously that have the largest commitment to that area of research are the National Science Foundation and the Environmental Protection Agency.

Miss SCHNEIDER. What is the status of coordinating that?

Dr. KINGSBURY. Well, the subcommittee has—there have been people suggested for membership on the subcommittee. It will be pulled together by Frank Harris, who is the Deputy Director of the Division of Biotic Systems and Resources of NSF. It will have heavy participation by the EPA research and development side.

Miss SCHNEIDER. The last question I wanted to ask you is: Does the administration have a position on user fees for biotech applications?

Dr. KINGSBURY. That is not something that we have discussed in detail. The discussions that have come up around user fees have been in the context of the Food and Drug Administration. Commissioner Young has testified regarding his attitude on the implementation of user fees. That has not been an issue that either the Domestic Policy Council Working Group or the BSCC has addressed.

Miss SCHNEIDER. Are you going to?

Dr. KINGSBURY. It is not currently on our agenda. It may come to our agenda. But it is not something that currently is on our agenda.

Miss SCHNEIDER. Well, I am interested in it from the fiscal point of view also, because the Department of Agriculture indicated that they were not interested in spending any more than $5,000 on an impact assessment, and I think that we have to sort of weigh where we're going to be spending those moneys, where they are anticipated coming from, et cetera.

Dr. KINGSBURY. Well, this is an issue that is extraordinarily complex, and while I have spoken with Commissioner Young about his philosophy, which I find, when he explains it, compelling, one concern that has been expressed by the industrial people is that in many cases some of the companies that are involved with some of these new products, especially in the plant sciences, are smaller companies, and the implementation of a significant user fee clearly impacts the smaller companies more than it does the Fortune 500's.

That has been a concern, so we are trying to balance—I think the notion has been to balance that. Again, this is not an issue that we have dealt with.

Miss SCHNEIDER. Well, I think that that certainly makes good sense, and so when you are dealing with this issue, I hope you will keep in mind that, yes, there are very small companies that are involved in this type of business as a business, essentially. But also I sure would not like to be on this committee when we do have a problem and find out that the Environmental Protection Agency did not do an assessment because they could not afford to do it, and so therefore the public welfare was not being protected.

So I think that if that is to be the case, then certainly you, among others, are going to have to come before Congress and say, "Congress, you must reorient your priorities and make sure that we have adequate funding for the Environmental Protection Agency, for NIH or the Department of Agriculture or whomever, so that we can, you know, implement our duty."

Dr. KINGSBURY. Yes. I understand.

Miss SCHNEIDER. I have no further questions, Mr. Chairman. Thank you.

Mr. SCHEUER. Congressman Harold Volkmer?

Mr. VOLKMER. Thank you very much, Mr. Chairman.

Dr. Kingsbury, what is the relationship between the Domestic Policy Council Working Group on Biotechnology and the BSCC?

Dr. KINGSBURY. The relationship is the following: During the development of the coordinated policy, one of the first questions that the Domestic Policy Council Working Group addressed—actually, at the time it was first addressed, it was the working—the Cabinet Council on Natural Resources and the Environment, which originally worked on the December 1984 policy statement. It then changed its identity as the White House has reorganized it.

The issue was central coordination and how to achieve central coordination. The original proposal in 1984 was for a strong central coordinating committee called the Biotechnology Sciences Board. That committee would have and was proposed to have very strong central powers and second-tier regulatory review. That was part of the proposal that went out for public comment, and the public comment that came back questioned the wisdom of that move. And as the committee reviewed the comments that came back from the public, it was clear that there were a number of problems introduced by a strong central board. The committee, the Domestic Policy Council Working Group, during its deliberations, decided that that was not an appropriate approach but that something that had senior agency members on it as the coordinating body that would coordinate the science and maintain a high level of agency interaction and agency discussion was the appropriate way to proceed without the second level of review.

So the Domestic Policy Council Working Group recommended as the first stage of the two-stage release of the policy, that the Biotechnology Sciences Coordinating Committee be established, and it was established within the FCCSET mechanism, and it was—its charter was published in the November 14 Federal Register.

So the short answer to—that was a long answer to your question—the short answer is that the BSCC is the child of the Domestic Policy Working Group, and it was the creation designed to be the scientific coordinating body, and that was its major and sole responsibility.

Mr. VOLKMER. All right. Now, the next question I have in regard to that is: Are all of the BSCC members also DPC Working Group members?

Dr. KINGSBURY. At the present time, that is the case, yes, sir.

Mr. VOLKMER. Then do the BSCC members, in effect, set science policy for the DPC Working Group and then analyze the science questions and issues for the BSCC?

Dr. KINGSBURY. The working group composition is quite a great deal different. The working group—the Domestic Policy Council Working Group—represents 18 agencies and executive offices. The BSCC only represents five. So that the incremental contribution of the BSCC members on the DPC Working Group is relatively small. The BSCC is dealing with a quite different set of questions. It does not deal with science policy. The BSCC has been dealing with questions strictly related to science. The policy questions that underlie approaches to regulation, underlie the policy statement as you see it, was really a question of the broad participation of the DPC Working Group, which had, as I said, 18 agencies represented, and is a very broad group that has active participation by all of the represented agencies and not just the five agencies.

Mr. VOLKMER. But relating just to the biotechnology field?

Dr. KINGSBURY. No, I think——

Mr. VOLKMER. Isn't the BSCC really the science policy determining body, and not the working group?

Dr. KINGSBURY. No, I would—I would not agree with that statement. I believe that the BSCC has attempted to stay out of policy and has focused on technical aspects, scientific aspects, that the biotechnology working group has as its sole responsibility biotechnology. It has a broad agenda of biotechnology questions; however, the principal focus in the last 2 years has been the coordinated framework.

Mr. VOLKMER. Well, is it policy or coordination or just pure science? In your statement, you say, "The BSCC will continue to have the primary responsibility for the scientific questions that arise in the future, including questions associated with risk assessment methodology and its further development and implementation"?

Dr. KINGSBURY. We consider that a question of science. We're talking about risk assessment methodology, not risk management methodology. We have dissociated those two and continue to dissociate them. That risk assessment is a scientific undertaking that does not—that provides the basis on which to make risk management decisions. And as I pointed out in here, the BSCC is not involved in questions of risk management; it's simply risk assessment methodology.

Mr. **Volkmer**. I agree with that.

Dr. **Kingsbury**. Very, very strict separation of those two activities.

Mr. **Volkmer**. I would like to go to one of the questions generally touched on by the gentlelady from Rhode Island. Now we get to the question in the question of methodology for risk assessment and the research of it, and how much funds are going to be going to it out of the total funds as against risk methodology for risk assessment and funds against development of biotechnology products and methodology for development of products.

That is facing us. Now, who is going to make that determination?

Dr. **Kingsbury**. Those are—and I believe that I, the last time that I was before you, made the comments regarding the setting of research priorities, and I have felt very strongly that those research priorities must be set by the research agencies and not by a central committee. We can encourage those agencies, we can have broad discussions between various members of the research agencies, but I feel that we can point those questions out. I am really reluctant to put the BSCC in the position of trying to set for the individual research funding agencies their priorities.

Certainly, I can speak from my point of view, and that is, within the National Science Foundation. I have argued strongly for adequate budgetary authority to enhance our program in risk assessment, to enhance our program in microbial ecology. This year, in fiscal year 1986, we increased the risk assessment research activity, which we have in the Social and Economic Sciences Division in the Decision and Management Sciences Program. We increased that activity by half a million dollars. These are basic studies in risk assessment methodology, not necessarily directed just to biotechnology but to broad risk assessment methodology.

Likewise, we have increased the amount of money available for—in the Division of Biotic Systems and Resources for basic studies in ecology and ecosystems.

I believe that it's true in the other agencies as well that there is a focus in this direction. So I think that it's safe to say that at least at the National Science Foundation the rate of growth of budget in the area of environmental biology that we see as providing basic information related to microbial ecology, that area of science in the National Science Foundation on a budgetary basis is growing a little bit faster than the area that one would identify as being further development of biotechnology itself.

Now, across all the agencies, of course, there is a balance, and the National Institutes of Health, of course, is not as heavily committed to environmental biology as we are. It's not their responsibility.

Mr. **Volkmer**. I would like to carry on with the same theme as to the question of coordination in science and the question of policy. You also stated in your statement that the BSCC considers this—that is, "necessary to regularly review the appropriateness of scientific basis of existing regulations"—I agree that that is. But the concluding "recommendations to modify existing statutes, if it is deemed necessary." Is that policy or science?

Dr. KINGSBURY. Those would be recommendations based on science. If we see——

Mr. VOLKMER. Now, wait a minute—well, you go ahead. Finish your answer. Go ahead, finish your answer.

Dr. KINGSBURY. We will be assessing the technology as it is being developed. We will see the direction that new products are going. Remember that one role that the BSCC is playing is to participate in discussions regarding new kinds of product applications that come into the agency and the means whereby the agencies feel it's appropriate for them to handle those, so that there will be discussion of specific applications and of questions that have arisen during review of specific applications.

Now, as I said today, we believe that the regulatory framework is appropriate for those products which we all see out there today and for things that we see coming down the pipeline. This is a rapidly changing technology. It is the role of the BSCC to review that technology, to continue to monitor what's going on. Remember that body is made up of not only the regulators but also the people who are funding the basic science, so that as new developments in basic science occur, people like Dr. Wyngaarden and myself will be aware of many of those developments, so that we will start to see changes in the scientific approaches and the kinds of potential new products that are coming available.

It's within that context that we will be able to say we see coming down the road potential problems of regulation because there are products that we had not anticipated. We then will be able to recommend that that question of how those should be regulated be reviewed. Now, whether it's the BSCC who comes forward with the recommendation or whether it's the agencies, I think that is a good question. I think that's the question you're addressing.

That's a place where it's a little hard to really be able to say where it's—it's one of those things that, if you're a scientist and you go to an international meeting and you hear somebody say something that just turns you on to a new idea and you go back in your lab and work on it, it's hard to identify where the idea came from, was it your idea or is it one you heard from someone else. I think that a little bit of what you're asking may be that kind of a—that kind of a question. Is it BSCC making the recommendation or might the Environmental Protection Agency be making it because Dr. Moore heard a discussion at a BSCC meeting that prompted him to think, "Gee, TSCA might not have a coverage"—or FIFRA, or whatever the statute might be?

So I think that you're asking a question that is a very difficult thing to come to grips with precisely.

Mr. VOLKMER. Well, that is one of—and if the chairman will give me a little more time; I know we have a vote on.

But what concerns me is, let's say that Dr. Moore or EPA or the Assistant Secretary over there, in reviewing FIFRA or TSCA, decides that, "Hey, we need a minor change or we need this little paragraph changed within the law." Can they come to the Congress or do they have to go through you first before anybody can say it?

Dr. KINGSBURY. Those are agency responsibilities and it's not the responsibility of the BSCC to be the clearinghouse. We believe that such questions would be discussed in the BSCC and the BSCC might make a recommendation. But we do not have the force of absolutely setting down the standard of how EPA does its business. EPA is an agency that has statutory responsibility to do that business, and that's the only way that they can fully proceed.

Mr. VOLKMER. All right. Again, are the scientific decisions that are discussed approved by the BSCC, and/or do they go to the DPC Working Group for approval?

Dr. KINGSBURY. Not necessarily. The BSCC is really not established to answer to the DPC Working Group. The DPC Working Group was formed with a very specific thing in mind, and it's now achieved most of its responsibility; and the Domestic Policy Council only chartered its working groups for finite time frames to do specific activities. Once those activities are over, those working groups may not be rechartered.

The BSCC was designed to live on regardless of what the Domestic Policy Council activities were, and in that sense it's not responsible to that body at all. It is a body that really is made up of the senior representatives of the agencies and is interactive and has a life of its own within the context of the FCCSET committee.

Mr. VOLKMER. Now, one thing—now I have some questions; I guess you are going to be on our next panel too, so I am going to save some of them for that.

As an example of your regulatory oversight role, you cite that it's widely—in your statement—"widely felt that gene deletions and intrageneric organisms pose no threat and therefore, should get only abbreviated review." How did you determine what was "widely felt"?

Dr. KINGSBURY. This was—without going into explicit details of the interactions——

Mr. VOLKMER. Let me try to abbreviate it.

Dr. KINGSBURY. OK.

Mr. VOLKMER. Was it widely felt within the BSCC, and that is determining widely felt; or is it widely felt by the scientific community across the spectrum in the United States, involving not only microbiologists and bacteriologists but also ecologists, et cetera?

Dr. KINGSBURY. It was widely felt outside of the BSCC. The precise makeup of the entire community that was polled I will not be willing to speculate on the number of ecologists who were polled on that question. There certainly were some. So we're talking about an attitude of the scientific community outside of just the BSCC.

Mr. VOLKMER. Did you get written comments?

Dr. KINGSBURY. The BSCC was only—the definitions that we have, as I point out in the testimony, were definitions that were derived in response to the publication in the December 1984 Federal Register notice. The Environmental Protection Agency received many comments regarding those proposed definitions that they had at the time, and as the definitions were refined, the Environmental Protection Agency continued to have comments from the scientific community. That is outlined on—in their policy statement in the Federal Register on page 23315. There is a rather substantial explanation of the public comments that the EPA received.

In response to that, the BSCC attempted to help EPA and Agriculture coordinate between them to come up with common definitions, and that was the—that was the point that the BSCC fully became involved. So there has been comment as it has been outlined in the Federal Register notice.

Mr. VOLKMER. All right. Now, will you be reviewing the regulations, proposed new regulations, by EPA and USDA; the BSCC, will they be reviewing those?

Dr. KINGSBURY. We have reviewed all of the documents so far, and it's my expectation that that would continue to be the case.

Mr. VOLKMER. Who recommended exclusion of noncoding regulatory sequences?

Dr. KINGSBURY. Who recommended that?

Mr. VOLKMER. Yes. EPA? BSCC? Where did that come from?

Dr. KINGSBURY. That is a question that I am absolutely—I am not absolutely certain that I can answer. It's back to the same question that I was referring to a minute ago. After a variety of discussions with people, one is never certain where the idea actually came from.

Mr. VOLKMER. Thank you.

Mr. SCHEUER. We have a rollcall vote on now. We will suspend for about 15 minutes.

[Brief recess.]

Mr. SCHEUER. Congressman Volkmer.

Mr. VOLKMER. Yes, Mr. Chairman. I had previously requested in one of my questions addressed to Dr. Kingsbury in regard to the source of some of the definitions, et cetera, and I understand he has some additional information he would like to provide us with. So at this time I would like for him to provide that.

Dr. KINGSBURY. I think that it would be worth mentioning as we talk about the language of the definitions and the exclusions of regulatory sequences and their concept of self-cloning. It was actually out of the changes in the derivation of the NIH guidelines that this notion was developed, and there were three or four portions to it. As the NIH guidelines developed over a period of time, one of the areas that was—the first area in which there was some retrenchment regarding the stringency of review of proposed recombinant DNA experiments was in the area of modification of regulatory sequences, self-cloning, introduction of sequences.

One of the first things that was in the NIH language was that the—the stringency of control of a particular clone was relaxed when it was known to be free of harmful sequences, it was characterized and known to be free of harmful sequences. The other portion of the NIH guidelines that is relevant here is the notion of the genetic exchangers list.

Now, these were all things that were considered during the discussions regarding the definitions. Because of the nature of the topics that we were dealing with, we felt that the language of the NIH guidelines—that is, "fully characterized and known to be free of harmful sequences"—was not precise enough for the regulatory environment, and so we chose not to recommend that that terminology be included, because that would have included coding sequences; that is, genes that would be expressed in the microorganisms if "they were known to be free of harmful sequences." Because of the nature of the ambiguity that was there in the context of regulation, we chose not to use that.

Likewise, the exchanger list, although many of us felt that it might be appropriate, was not included, but it is one that is subject to comment. We're asking for that. And it might be subject to EPA rulemaking.

So much of the approach that one sees in the definitions as an approach, the original ground was cut for that by the NIH during the process of the derivation of the NIH guidelines. This was not totally a new approach, but in fact mimicked that.

Mr. VOLKMER. And are you saying basically for a layman that it's an extension of the NIH——

Dr. KINGSBURY. That's right.

Mr. VOLKMER [countinuing]. Procedure from the time that they started in the review process to where they are now——

Dr. KINGSBURY. That's right.

Mr. VOLKMER [continuing]. And you're just extending that?

Dr. KINGSBURY. That's right. That's right. It was a concept that was developed during the development of the NIH guidelines. And we simply have adhered to that notion and extended it into this area.

Mr. VOLKMER. OK. Dr. Kingsbury, you mentioned in commenting the EPA rules and regulations, we know they're coming. At the time that the guidelines were being developed and prior to their being placed in the Federal Register and open to the public, were they reviewed by OMB?

Dr. KINGSBURY. I would say—the document—the Federal Register notice reviewed by OMB?

Mr. VOLKMER. Yes.

Dr. KINGSBURY. It went—a copy—OMB was a participant in the DPC Working Group.

Mr. VOLKMER. OK. The next question I have—I am not very concerned about that as much as I am about what my next question is. EPA and USDA are now proposing rulemaking. Will those be submitted by you all to—your group—to OMB?

Dr. KINGSBURY. The individual agency statements by the agencies would be submitted as part of their standard agency clearance process.

Mr. VOLKMER. I recognize that. But will you yourself or the BSCC have contact with OMB in regard to those proposed rules?

Dr. KINGSBURY. It is not—our responsibility is to coordinate at the agency level, and that's how we work. It's a body made up of senior agency officials, and our coordination and consensus-building is done at that level, and it's the individual agency responsibilities, then, to carry forward with their rulemaking and their policy. So we would not be the ones that would submit that to OMB, but in fact it would be the individual agencies that did that. We have no responsibility in that sense to deal with the OMB.

Mr. VOLKMER. So basically then there would be no informal discussions with OMB on those either, by the BSCC?

Dr. KINGSBURY. BSCC does not have an OMB membership.

Mr. VOLKMER. Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you, Congressman.

Dr. Kingsbury, the purpose of these guidelines, or certainly one of the purposes of these guidelines, was to provide certainty and finality on this whole host of biotechnology issues. Yet, as I noted in my opening statement, major questions remain unresolved. In fact, the more one looks at the guidelines, the more questions seem to be open and unresolved.

For example, large part—large parts of the Department of Agriculture and EPA's regulations depend on the completion of rulemaking which may be several years away. It seems to me this is just symbolic of uncertainty and confusion that is rampant, that runs throughout the guidelines.

Has this uncertainty resulted from the administration's grave reluctance to consider new legislation giving the agencies the authority that they need to cope with the obvious regulatory challenge presented by this whole new science of biotechnology and genetic engineering which nobody dreamed of when we passed the present regulatory format?

Dr. KINGSBURY. You are asking a couple of questions there which border on legal issues which I am not really qualified to comment on.

Mr. SCHEUER. No, I am asking you a question of judgment, not the law.

Dr. KINGSBURY. Well, I will try to handle those. It was—the question of judgment, I think, as the policy was derived, it was the judgment of the working group over the entire 2-year period or 2½-year period of the policy development, that there was an adequate statutory base to pull together the regulations for the industry.

The problem that one faces is that in some instances the statutes that were being used do require rulemaking for full implementation, and so there was—there was the potential of some delay as those rules were promulgated. The public had full opportunity to comment. And so we do see instances here in the policy where, in the case of Agriculture, in particular, there are requirements for rules. Now, the proposed rules are here——

Mr. SCHEUER. Isn't there a very real doubt as to whether they have the authority, the legal authority, under their existing legislative mandate to engage in rulemaking on genetic engineering? This is what we have wanted to clarify.

Dr. KINGSBURY. Yes.

Mr. SCHEUER. And it seems to me that—that these rules, this rulemaking on which you have labored for several years, does nothing but further compound and confuse an already very complicated——

Dr. KINGSBURY. Yes.

Mr. SCHEUER [continuing]. And puzzling situation.

Dr. KINGSBURY. Let me simply make the comment that the first exercise when we began, I was present at the original meeting of the working group in April 1984. The first exercise that we engaged in was a complex review of the statutory base that was available. That was a review that was generated by the general counsels from each of the agencies, with explanations and comments on the statutes that applied to those agencies. It was reviewed by the general counsels as a group, if I am not mistaken. It's certainly that by the working group, which includes representatives from the Justice Department.

We worked on the basis of the legal opinion that came from that group, and I have to trust them because that's not my area of expertise. It was their consideration that the statutory base, as it existed, was appropriate and these statutes could be applied to biotechnology. It was that conclusion that we worked from throughout the process.

So I simply would have to comment that the judgment that we made was based on the best advice that we could obtain from legal counsel, and that the statutory base was adequate.

Mr. **Scheuer**. Isn't it true that until the final EPA rules are in place several years from now, EPA has no current authority whatsoever even to—even to require notification for releases of many genetically engineered organisms into the environment, they can't even require that they be notified; isn't that true?

Dr. **Kingsbury**. It's my understanding—and we're moving into an area of legal interpretation which I am not fully competent to deal with—but it's my understanding that the policy that currently exists applies the Toxic Substances Control Act, to new organisms as defined in the EPA statement, and that they are immediately subject to premanufacturing notification.

The area that is not covered absolutely right now is the area that would be covered under their significant new use rule. They're asking for voluntary compliance with the intent of the significant new use rule, and I know that they're in the process of preparing it.

Mr. **Scheuer**. I want you to put yourself in the shoes of a businessman who has just received from the Government a copy of your rulemaking. Now I am going to read here: "EPA has authority for all"—and this is at the top of page 23306.

Dr. **Kingsbury**. 306?

Mr. **Scheuer**. "EPA has authority for all environmental research on microbial pesticides, regardless of whether research is federally funded or not. EPA will regulate research under a two-level review system based on its evaluation of the potential risk posed by various types of microorganisms with lesser notification required for level I reporting and full review for level II."

Fair enough. Now we go on: "For other uses"—"For the other-uses category from chart II, research involving nonpesticide microorganisms released into the environment. Jurisdiction for release may be under S and E,—that's the Science and Education Division of USDA, the research arm of USDA, NSF, the National Science Foundation, APHIS, the Animal and Plant Health Inspection Service of the U.S. Department of Agriculture, the regulatory arm of USDA, or the EPA, depending primarily upon the source of funding, but also upon the purpose of the research and the characteristics of the genetically engineered microorganisms."

Would that puzzle you if you were a businessman as to where to go for advice and counsel?

Let's go on. "This genetically funded research conducted for an agricultural"—"Thus, genetically funded research conducted for an agricultural use will require adherence to S and E guidelines and approval of certain experiments by S and E or NIH, depending upon which is the funding agency. EPA will review commercial research. APHIS's jurisdiction applies to issuing permits for regulated articles, plant pests, or animal pathogens."

Can you imagine the absolute morass in which a businessman or a business executive would feel himself to be sinking, having just read a paragraph like this? Where do they go for help?

Dr. KINGSBURY. Well, unfortunately, my phone number is on page 33202, and that has been the pattern that has been followed by many people. [Laughter.]

Mr. SCHEUER. From a commonsense point of view——

Dr. KINGSBURY. Yes. Well, let——

Mr. SCHEUER [continuing]. What was already a puzzling and confusing situation, it seems to me, is a situation that has only been compounded by the issuance of these regulations.

Dr. KINGSBURY. Well, we're talking here about the research side of regulation, and I think that these were caveats that were—which were designed for clarification of chart II, which is fairly straightforward. If you have Federal funding, you are responsible to the agency which funds your research. I made a comment to that in my testimony. I think it's very clear, and that's unequivocal. If you have an NIH grant, then you deal with the NIH. I think that that is very clear for anybody, and I think the scientific community is very accustomed to that notion.

Mr. SCHEUER. And how many other agencies might you have to deal with besides NIH?

Dr. KINGSBURY. The NIH will make a decision as to which committee is the appropriate committee to review that environmental release, and that is the only other agency to which you would be responsible, for a federally funded research activity. That part of it is very straightforward.

Nonfederally funded research falls within the EPA. There are instances in which one might be working with an animal pathogen. Animal pathogens—excuse me, plant pathogens. Plant pathogens fall under the Federal Plant Pest Act and have to be registered with APHIS. That is not a new part of this coordinated framework; that has been the case for a very long time.

There are a large variety of both animal and plant pathogens which require having an APHIS permit. That's been true for as long as I have been involved in scientific research.

For example, it's been well known that—I happen to work with an agent called the scrapie virus; it's an animal pathogen, it's controlled, and we've had to have permits to move it from one place to another for a long time. That's part of what's referred to here. That is not new as part of this regulation. It was pointed out here simply to reiterate to those, especially in the academic community who do not always recognize the fact that these are controlled activities.

I understand the point you're making about the complexity of the language, but I think the charts together with the language are fairly straightforward.

Mr. PACKARD. Would the gentleman yield, please?

Mr. SCHEUER. Surely.

Mr. PACKARD. I think that to the novice and to the uninformed and those that are not involved in this process, regulations are always complex, and certainly these would be complex to the nonscientist and to the nonresearcher. But to the researchers, I think they have been crying for guidelines and they would rather have guidelines that their scientists can get into, and they will understand them, in my judgment, even though you and I may not, because of our backgrounds.

But I think that they generally will be able to understand the guidelines and are welcoming the guidelines now. If there are some complexities, they will certainly, I think, inquire and find out how—what the guidelines are telling them to do. It really doesn't bother me so much whether the language is complex to us. What bothers me, of course, is if in fact the guidelines have voids and loopholes that need to be covered.

Mr. SCHEUER. Well, we're going to hear from some researchers in the next panel, and we will hear whether they have any concerns or not.

But it seems to me that the guidelines are so absent of clear definition and have so absent clear locus of authority in defining, in making the definitions, that if I were a businessman and I were the chief executive officer of a biotechnology engineering firm, I would be hard-pressed to conclude that I could operate in this environment that has been spelled out in these guidelines in a businesslike way. I would be hard-pressed to feel there were certain places where I could go for answers and be told this is what you have to do to release a genetically engineered substance into the environment and if you do that you're home free. And that's what a businessman needs to know.

What we're trying to do is to liberate the business community to know what is required of it, to know the standards that they have to meet, to know the procedures they have to meet so they can go ahead and do their thing. It doesn't seem to me that that happens—that that is happening in these guidelines.

Dr. Kingsbury, you testified that developing a definition of "contained facility" is the job of a subcommittee of the BSCC. How often has this subcommittee met?

Dr. KINGSBURY. Let me, if I may, answer that question a little more broadly.

Mr. SCHEUER. No, no, no. Just give me a simple answer. Has it met once, twice, three times; weekly, monthly, annually? How many times has it met? And then you can elaborate.

Dr. KINGSBURY. OK. It has met once that I can absolutely assure you of, and I am not—I believe that it has met twice. So, one or two is the answer.

Mr. SCHEUER. It had a meeting in July, and in your—in the remarks you made on July 9 in the auditorium of the National Academy of Sciences you said this was really an organizational meeting of the committee. This is the committee on risk assessment.

Dr. KINGSBURY. Oh, I am sorry. The risk—yes, that was a different—OK. The risk assessment committee has had—the risk assessment committee has had an organizational meeting and the final membership is now being put in place. They expanded its membership. The greenhouse committee is what I thought you were asking about.

Mr. SCHEUER. No, no. I am.

Dr. KINGSBURY. OK.

Mr. SCHEUER. But you mentioned that the risk assessment committee, on page 4 of your testimony, has probably—and I quote you—"has probably been the most active subcommittee so far." Now, if they've had one meeting and they're the most active subcommittee——

Dr. KINGSBURY. I am sorry, you're talking about the draft from the public meeting?

Mr. SCHEUER. Yes, I am talking about the transcript from——

Dr. KINGSBURY. The transcript for the public meeting, not the testimony. Yes, sir. All right.

Mr. SCHEUER. Yes.

Dr. KINGSBURY. I understand.

Mr. SCHEUER. You mentioned the risk assessment committee met once and that it was the most active subcommittee so far. Now, if that's true—and I certainly take you at your word——

Dr. KINGSBURY. Yes.

Mr. SCHEUER [continuing]. Tell us how did the subcommittee of the BSCC that was supposed to work on the definition of "contained facility," how has it approached that job? How many meetings has it had? What is its staff? What is its backup? How much research was done? Who sits on that committee? What has been the process of deliberation, and the formulation of that—of that definition of "contained facility"?

Dr. KINGSBURY. OK. Now, the BSCC subcommittees have not been in existence for the same length of time that the BSCC has been in existence. The BSCC was chartered and began its activities on October 31. During the early period of the BSCC it met approximately monthly and deliberated as a single body without subcommittees on a variety of issues, which included the definitions and a number of other issues, including the determination of how that committee wanted to proceed into the future.

We are talking about a committee that at this point is about 9 months in existence. The early stages of the BSCC were very much taken with its initial activity of dealing with some of the scientific questions that were coming to the committee as part of the referrals that came during the development of the original policy.

We also at that time were making——

Mr. SCHEUER. Dr. Kingsbury, you have been 2 years at work.

Dr. KINGSBURY. No, no. No, no. I was just pointing out that the BSCC was only chartered and began meeting October 31. It's 9 months old, 8½ months old now. I am talking about——

Mr. SCHEUER. The Domestic Policy Council has been working for 2 years——

Dr. KINGSBURY. Yes, sir.

Mr. SCHEUER [continuing]. At developing guidelines.

Dr. KINGSBURY. Yes, sir.

Mr. SCHEUER. Now, you still don't have a definition of "contained facility." You still have done virtually nothing on risk assessment, which is the basic science of appraising the risk of releasing these genetically engineered substances in the environment. It seems to me you have labored long and——

Dr. KINGSBURY. No, no, I think if I——

Mr. SCHEUER [continuing]. And come forth with a mess.

Dr. **Kingsbury**. If I could—if I could correct you at one point, there is in fact a definition of "contained," and that's the approach that we have actually come from in the EPA document. The EPA deals with the concept of "contained." That is, it's a very conservative notion, and so in fact they use "contained" as their standard. So in that sense, they have a working definition of "contained."

The question that we have been working on is, in fact, the opposite. We are asking questions as to whether that definition, which is a very conservative definition, is an appropriate one to continue with. And so the question that we're dealing within the subcommittee is the question of release, as contrasted to containment. Those two go together. So in fact we have a very conservative definition for "contained" in place.

Now, the DPC working group as a body was not focussing on those particular issues. Those were science issues that were at the agency level. The BSCC came in to help coordinate between the agencies.

Mr. **Scheuer**. I must confess I am confused. On page 23335, at the bottom, the very bottom of the first paragraph, (d), "How to determine if a product is released to the environment", it says, "A microorganism will be considered environmentally contained if the microorganism is used in a laboratory that complies with NIH/RAC guidelines."

Dr. **Kingsbury**. Yes. That's straightforward, I think.

Mr. **Scheuer**. "When a microorganism is used in a contained greenhouse, fermenter or other contained structure, building or structure that has a roof and walls." I have difficulty working with that one, and perhaps it's my lack of scientific background. Anyway, we will get on with these questions, more of them, in the next panel.

In the meantime, Congressman Ron Packard.

Mr. **Packard**. Thank you, Mr. Chairman.

I would like to pursue briefly what the chairman was just inquiring about as to the clarity of the guidelines and ask a simple question, I think, paralleling his question.

In your judgment, are the guidelines clear enough so that industry will be able to comply? The thing that we don't want is for another rooftop experiment or another inoculation of pigs that they feel they were complying and yet, in fact, they weren't. Do you think they're clear enough?

Dr. **Kingsbury**. It's our feeling that they are clear and that the industry and the academic community understands what's there. I believe—again it may be a matter of perspective—but the portion that the chairman just read seemed clear to me. I mean, we think that they're clear. I think that, you know, you may be asking the wrong people, and I would recommend that—I notice that one of your panels this afternoon has an industrial representative, and I think it would be appropriate to get their impression of the clarity from their point of view.

Certainly, as I mentioned, in the Federal Register there is essentially an information hotline, and that is that when people are confused they have a place to call. There have been a couple of calls. The calls have indicated that the callers have had a great deal of insight into the questions of the—of the guidelines. In fact, the questions that I have been faced with have all been particularly difficult ones that really dealt with the nuances and not the big picture. Generally, I think, people have understood the structure.

Mr. **Packard**. What kind of educational procedures are intended by the agencies to make certain that these guidelines now become available and familiar to those that would be interested in making application?

Dr. **Kingsbury**. Well, there have been, as I mentioned in the testimony, some briefings for the—for the general public and for the industry. Certainly, there has been very wide distribution of the documents. In terms of any other specific—agency-specific—activities, I would defer to the individual agencies for their plans. I am not absolutely certain what each of the agencies intend.

I do know, as it is announced in here, that the Agriculture Department is planning public meetings to discuss the guidelines. There is one next Tuesday in Sacramento, for example. There will be others, I understand, here in Washington, in St. Louis, and probably San Francisco.

Mr. **Packard**. One of the areas of concern is the small-business exemptions in TSCA's jurisdiction. How do you—how will that play out in terms of small-business exemptions? What will they be required to do? What will they be exempted from doing?

Dr. **Kingsbury**. That's an area that is a little bit, I am afraid, technical from my point of view in terms of TSCA law. One of the things that I am trying to understand is TSCA law, but I do not—I am not an expert. That is subject to additional rulemaking, as I understand it. It is—and I think it would be appropriate to ask Dr. Moore later on. But it's my understanding that there would not be—that there would not be an unusual exception for environmental release, that the small business would be under the same regulations that anybody else would be.

Mr. **Packard**. One of the concerns also in business and in industry is competition from foreign sources, and one of the purposes of trying to develop these guidelines is to allow our own domestic industries to compete and not to see a lot of our research go abroad.

How do the guidelines deal with the products or research from foreign sources, foreign institutions and foreign companies?

Dr. **Kingsbury**. Well, the requirements certainly are consistent for all producers regardless of where they would be. I mean, the standards of introducing a product into the United States, regardless of where the product came from, would be the same.

We, because of the fact that we recognize that the world trading system is an important aspect of our developing industry and that we are the world leaders, we are particularly interested in cooperation across multinational boundaries to have coordination of the regulatory environment with the OECD and the European Community, and we have been working toward that end so that there is consistency for the regulatory approach for products that are developed in the United States as they go overseas and overseas companies as they come into the States.

Mr. **Packard**. Do you see any area in the guidelines that would induce companies to go overseas to produce their marketable products or to do their research, anything in the guidelines that would induce them to do that, outside of economics?

Dr. **Kingsbury**. We hope there is not. Certainly, this was an issue that has been discussed in a number of instances, the fact that people would be sent offshore for some of their research. We believe that this is a clear and rational regulatory policy that would not entice the producers in the corporations that are in this industry to move offshore.

We think that these are guidelines that allow for rational progress, that allow for a reasonable progression from research through testing and development for companies, that it is as rational as those anywhere else in the country, and we believe—it's our hope—that it clarifies the situation. I am acknowledging that not everyone seems to think that. But we believe that it would clarify the situation such that American industry would feel comfortable continuing to do their work in the United States and that the public would feel confident that we had put together a regulatory matrix that would not—would not give any enticement for people to go outside of the country.

Mr. **Packard**. Would you be kind enough to clarify exactly what products and what research would not be subject to the level—or any level—of review; for example, nonpathogenic single-gene deletions, the nonfederally funded, noncommercial or nonacademic research or field research?

Dr. **Kingsbury**. Yes.

Mr. **Packard**. I would be interested to know precisely what is not going to be required for review.

Dr. **Kingsbury**. I think on page 23319 in the Environmental Protection Agency statement they have a summary table that reviews microorganisms applied to the environment, and within that table they break it down into FIFRA and TSCA. And one will notice that they have identified two levels of review and two levels of field testing. Within that context, under TSCA, every class of microorganism, regardless of its manipulation, would be subject to some form of review.

Some of those reviews are extensive reviews; others are abbreviated reviews. But all of those organisms would be subject to review prior to introduction into the environment.

Within the area of FIFRA, you will notice that there are two classes of microorganisms that are not subject to review when used under 10 acres, but when used in 10 acres or more, would be subject to review. So we're talking about a very stringent review process in which virtually every organism that would be introduced into the environment would have one form of review or the other. That would include gene deletions, as people have asked. There is a level of review for gene deletions. But it is not the full review, but it's a notification review. It's not a premanufacturing notification.

Mr. **Packard**. That would also include nonfederally or noncommercial——

Dr. **Kingsbury**. That's correct. Any introduction into the environment, whether it's federally funded or not federally funded, is subject to review.

Mr. **Packard**. Also, we note that some of the guidelines take effect immediately and some are going to have to wait for some rulemaking to take place. How long do you anticipate before the rulemaking process is completed to where all the guidelines are in effect?

Dr. KINGSBURY. The—as you know, the APHIS guidelines, the APHIS proposed rules, were included with this Federal Register notice. There are some rulemakings that come from the EPA which were not included here. I am not the best person to try to speculate on how long it's going to be before the EPA's rules—the proposed rules appear. I know they are anxious to move ahead rapidly and to get them in place.

I would like just to refer that if I may to Dr. Moore.

Mr. PACKARD. What effect do you think those delays will have on industry in their applications?

Dr. KINGSBURY. EPA has requested voluntary compliance, and it's my intent—it's my impression that industry will voluntarily comply. So that in effect, those rules are in place, certainly in practice. I know that they're planning to move ahead quickly. I don't believe that those delays are going to have a significant impact, for two reasons: First is that the pipeline of products in those classes appears to be very—there are very, very few products that fall within the classes of organism that are subject to the rulemaking, so that the number of products that we envision is very, very small, if there are any there at all. So we believe that that delay is not going to be serious. Again, we've—they've—the EPA has asked for and, I think, will get voluntary compliance with that portion of the document.

Mr. PACKARD. I think one of the concerns by industry and our institutions, academic institutions and others that are doing research, is the unsettled atmosphere that has existed and certainly appears will continue to exist during the rulemaking process. Also, EPA's definitions have generally been well—been effective, and yet we're also opening now for and soliciting comments, public comments—BSCC is—for a period of time.

Do we anticipate that those definitions still remain in an unsettled position where the comments, the public comments, could alter the definition and thus a further unsettling of understanding by those that will be doing the research?

Dr. KINGSBURY. Well, the EPA's definitions are in effect now. The BSCC, as the science body, is taking the approach that scientists take, and that is to continue to consider the kinds of questions that arise as a result of any kind of scientific interpretation.

We want to hear what people have to say. If there are very serious issues regarding the definitions and those issues are identified by the BSCC and we are very concerned, there is the potential that we could go back to the EPA and point those out to them and say you might want to consider making this change. So that's not impossible. We don't really believe, given the nature of these definitions, that there would be dramatic changes, so that the definition of a pathogen, for example, does not seem to be at all controversial. So we do not see dramatic changes that I would envision as being unsettling.

Mr. PACKARD. One quick question. Miss Schneider, in her opening remarks mentioned a balanced policy that would protect the environment and human safety and yet at the same time not produce impediments to the ongoing development and research aspects.

Do you think these guidelines will reach that balance?

Dr. KINGSBURY. I believe that that balance is achieved here. I think there are many certainly—speaking from a personal viewpoint, and I am not trying to represent the position here of any of the committees; I am disassociating myself from them, having to live with the statement I will make. Certainly there are members of the scientific community who I know as a microbial geneticists who have commented to me that they think we have erred on the side of being too conservative.

Mr. PACKARD. Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you very much, Dr. Kingsbury. We appreciate your testimony.

We will now have the second panel—oh, Congressman Ritter, did you have any questions?

Mr. RITTER. Mr. Chairman, I did not have any questions at this time. Thank you.

Mr. SCHEUER. Thank you.

All right, we will now move to the second panel: Dr. Monica Riley, Professor of Biochemistry at the State University of New York at Stony Brook, and also representing the American Society for Microbiology. She is also chairman of the Committee on Genetic and Molecular Microbiology of the Public and Scientific Affairs Board. Dr. Margaret Mellon, director of the Toxics Program of the Environmental Law Institute; and Dr. Elliott A. Norse, of the Ecological Society of America.

Dr. Kingsbury—that's right—Dr. Kingsbury will remain at the witness table and will be available for questions.

OK. We are going to hear first from Dr. Margaret Mellon, director of the Toxics Program of the Environmental Law Institute.

Dr. Mellon, since we are running a little bit late, why don't you all take about 5 or 6 minutes to summarize your testimony—hopefully not trying to read it—and then I am sure we will all have some questions for you.

Dr. Mellon.

STATEMENT OF DR. MARGARET MELLON, DIRECTOR, TOXICS SUBSTANCES PROGRAM, ENVIRONMENTAL LAW INSTITUTE

Dr. MELLON. Good morning. My name is Margaret Mellon, and I am the director of the Toxic Substances Program at the Environmental Law Institute.[1] My remarks this morning will focus on two sections of—two sections of the framework document, the statement of the Biotechnology Science Coordinating Committee and the policy and regulations proposed by the Department of Agriculture. I will begin with the BSCC statement.

The BSCC appears poised to play a central role in the regulation of biotechnology. Before the BSCC proceeds much further in this role, it is important to clarify the scope of its authority and the range of its permissible activities. According to the statement announcing its formation, the BSCC is intended to serve merely as a coordinating forum on biotechnology policy issues.

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[1] See appendix 10, p. 282.

It is worthwhile to note that the BSCC appears to have no regulatory authority. It has not been charged by Congress with the administration of any of the environmental statutes. In the statement announcing its formation, the only authority claimed for it was that derived from the Federal Coordinating Council for Science, Engineering and Technology. Where a new technology impacts the territory of several major agencies, coordination is a legitimate and a needed function, but where an agency, without authority, sets about coordinating agencies with substantial authority, there can arise a temptation to impose positions on the coordinated agencies, often in the name of consistency. This temptation should be avoided.

In matters that have regulatory significance, the imposition by the BSCC of its position on member agencies could constitute an improper usurpation of authority. Such usurpation is of special concern because of the BSCC's tendency to meet and reach its decisions behind closed doors without keeping adequate records of its deliberations.

According to the coordinated framework, the BSCC has acted or intends to act on at least two definitional matters that are arguably of regulatory significance. The first is the definition of "engineered organisms" and the exemptions therefrom; the other is the definition of the term "release." Although scientific in content, these are purely regulatory in impact. Especially in the case of USDA and EPA, these definitions determine the scope of regulation under existing statutes. Defining the scope of statutory authority is properly the function of the agency charged by Congress with the administration of the statute.

The status of the BSCC's recommendations on these definitions and other matters of regulatory significance should be made clear. It would appear that unless and until they are adopted by respective agencies in accordance with proper procedures, such definitions are merely suggestions. If any of the affected agencies chooses to modify the definitions, it would appear to be within its power.

I would now like to move to a discussion of the policy of the Department of Agriculture. I would like to begin by noting that of the agencies faced with the development of biotechnology programs, the Department of Agriculture has had, by far, the most difficult task. Unlike EPA or FDA, USDA administers a diffuse group of statutes that generally do not limit USDA to particular products, applications, or activities.

As a result, USDA was required to develop a comprehensive policy covering research, commercial research, development—commercial research and development and commercial use of all agricultural applications to plants, animals, and microbes. It was a broad charge, and the USDA policy shows a lot of hard work in meeting it. But the USDA policy falls short in several major respects. These concern the scope of coverage, the quality of the review offered, the coordination within the agency, and its statutory mandate.

In general, the USDA scheme appears for the most part to leave unregulated the commercial research and use of products of agricultural biotechnology except insofar as the companies choose voluntarily to submit the products or the experiments to USDA's ABRAC.

In the two instances where an enforceable regulatory regime will be imposed, the VSTA and the Plant Pest Act, that regulation appears not to be addressed to the scientific issues that have precipitated the interest in genetic engineering.

I would like to turn to the regulation—to the regulatory policy proposed under the Plant Pest Act. USDA apparently intends to assert enforceable authority over only one major category of organisms: plant pests, as defined under the Plant Pest Act. This definition includes, among other organisms, mites, nematodes, insects, and other invertebrates, but covers these organisms only if they are plant pests. It does not include them if they are beneficial to plants. It does not cover, regardless of the impact on plants or anything else, nonparasitic plants, that is, that's most of the plant world, or vertebrate animals, including fish, frogs, poultry, and livestock.

In USDA's opinion, organisms that are not plant pests simply do not need to be regulated. I quote from the policy statement: "Other genetically engineered organisms which are engineered from certain organisms which are not plant or pests are classified in taxa which do not contain plant pests need not be regulated." This is a remarkable statement. Apparently, APHIS believes as a scientific matter that only those genetically engineered organisms that are plant pests pose a threat to the environment. If so, APHIS's position is at odds with that of much of the scientific community. It is also a position that is inconsistent with the USDA's ABRAC research policy, which describes list upon list of organisms that need regulatory oversight.

It should be noted that the APHIS position does not appear to be the reluctant result of the limitations on its jurisdiction imposed by the Plant Pest Act. APHIS is not chafing at the bit of that jurisdiction. It appears to have embraced those restrictions as the lines along which a scientifically defensible policy can be developed.

Now, scientifically, the policy totally misses the mark. As the ABRAC guidelines demonstrate, there are numerous organisms outside the confines of the plant pest category that are of concern and that should be reviewed for their environmental impact prior to release.

In the interest of time, maybe I will move to the end.

Mr. VOLKMER [presiding]. I would appreciate that. You go ahead and review your statement. I think it's very important.

Dr. MELLON. Pardon?

Mr. VOLKMER. You go ahead with the rest of your statement—I think it's very important—rather than skipping to the end.

Dr. MELLON. Oh. All right.

The quality of the review under the Plant Pest Act:

Even where the USDA is asserting its regulatory authority, the reviews it intends to perform are going to be perfunctory and inadequate to address issues of ecological safety. According to the Federal Register notice, the review performed under the Plant Pest Act is aimed at determining whether an organism is a plant pest.

In that document, the USDA estimates that the information required to obtain a permit will cost only $5,000 to prepare, and will not require the generation of any new data. The required information will include, among other things, descriptive data, country of origin, and quantities of planned introductions.

While the notice claims that the information is supposed to be sufficient to allow USDA to assess the behavior of organisms in the environment, it will not be possible to do so with any degree of thoroughness with that kind of information. None of the information on competitiveness or survival that is needed by other agencies, like the EPA, is asked for by USDA. It is scientifically impossible to understand how USDA could make an assessment of ecological hazard without ever requiring additional case-specific data.

The APHIS review may allow the agency to make a determination of whether a plant is likely to be a plant pest, but in most cases, in my opinion, that determination would be a waste of $5,000. The objective of the regulatory review scheme is simply irrelevant to the mainstream scientific concerns about genetic engineering. Plant pests are part, but only a small part, of the problem. Restricting the movement of and inspecting and carefully packaging plant pests does not address the real problem.

Moreover, other than herbicides, it would not seem likely that many plant pests are going to be intentionally produced. Of much greater concerns are organisms that are intended to do something beneficial and are therefore planned for release in large numbers into the environment. Under this approach, these organisms will not be reviewed or regulated at all.

Lack of a mandate to protect the environment: The APHIS approach raises many questions about USDA's ability to protect broad environmental interests in the area of genetic engineering. As the USDA policy makes explicit, USDA's mandate is to protect and enhance agriculture and forestry in the United States. APHIS's narrow approach to the regulation of biotechnology is fully consistent with this view of its mandate, but an adequate response to the release of genetically engineered organisms demands a concern for the total environment, not just for the agro-ecosystem.

USDA's caution with regard to its mandate is justified. Congress has not charged USDA with protecting broad environmental interests. If it were to have stepped out boldly to protect the environment, it would have nothing to stand on except for the National Environmental Policy Act. And I think that would have proved to be a thin basis for a strong regulatory program.

This lack of mandate is the source of a gaping hole in the current biotechnology framework. EPA has such a mandate and is the better choice for the agency to regulate the broad environmental impacts of—the broad impacts of the agricultural applications of biotechnology. But if Congress wants USDA to take on the task, new legislation mandating the protection of the environment as well as agricultural interests will be needed.

One final point about the framework document. It disturbs me that the biotechnology policy pays very little attention to what appears to many to be the central feature of the deliberate-release issue: its scientific uncertainty. Scientists have not yet determined whether or not the release of engineered organisms represents a serious economic and environmental threat. In the absence of data, plausible scientific cases can be made to support both positions. This is the soft sort of underbelly of the entire deliberate-release issue. If the Federal Government chooses to control the technology at this early stage before its risks are understood, it must also attempt to resolve the uncertainty about the nature of those risks.

The answers to the questions, to the scientific questions, will not automatically fall out of the process of regulation. Understanding the nature of ecological risks must be made a regulatory goal that is specifically articulated and adequately funded.

Thank you.

[The prepared statement of Dr. Mellon follows:]

TESTIMONY
of
Margaret G. Mellon

Before the Subcommittee on Natural Resources,
Agriculture Research and Environment, the Subcommittee on
Investigations and Oversight, and the Subcommittee on
Science, Research and Technology of the Committee on
Science and Technology

July 23, 1986

INTRODUCTION

My name is Margaret Mellon and I am the Director of the Toxic Substances Program of the Environmental Law Institute. I was trained as a scientist and have done post-doctoral work in molecular virology. I am also an attorney who has practiced environmental law. I am very pleased to have this opportunity to comment on the recently released Coordinated Framework for the Regulation of Biotechnology. The Environmental Law Institute is a nonprofit, non-partisan research and educational organization dedicated to the improvement of environmental law and policy. ELI regards biotechnology as a powerful force that in the coming decades will have a major influence on global social, environmental and economic developments. It views the next few years as a golden, but fast-evaporating, opportunity to put in place a reasonable apparatus to evaluate and respond to the technology.

My remarks focus primarily on two sections of the framework document: the statement of the Biotechnology Science Coordinating Committee and the policy and regulations proposed by the Department of Agriculture.

I. BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE

The first section of the framework document is the product of the Biotechnology Science Coordinating Committee (BSCC), the newly organized coordinating entity established by the Office of Science and Technology Policy (OSTP) under the Federal Coordination Council for Science Engineering and Technology (FCCSET).

ELI has two comments on this section, one procedural and one substantive.

A. The Limits of the Authority of the BSCC

The procedural point concerns the scope of the authority of the BSCC. The BSCC appears poised to play a central role in the regulation of biotechnology. Before the BSCC proceeds much further in this role, it is important to clarify the scope of its authority and the range of its permissible activities.

According to the statement announcing its formation, the BSCC is intended to serve merely as a coordinating forum on biotechnology policy issues. It is worthwhile to note that the BSCC appears to have no regulatory authority. It has not been charged by Congress with the administration of any of the environmental statutes. In the statement announcing its formation, the only authority claimed for it was that derived from the FCCSET.

Where a new technology impacts the territory of several major agencies, coordination is a legitimate and needed function. But where an agency without authority sets about coordinating agencies with substantial authority, there can arise a temptation to impose positions on the coordinated agencies, often in the name of consistency. This temptation should be avoided. In matters that have regulatory significance, the imposition by the BSCC of its position on its member agencies could constitute an improper usurpation of authority. Such usurpation is of special concern because of the BSCC's tendency to meet and reach its decisions behind closed doors without keeping records of its deliberations.

According to the Coordinated Framework, the BSCC has acted or intends to act on two definitional matters that are arguably of regulatory significance. The first is the definition of engineered organisms and the exemptions therefrom; the other is the definition of the term "release." Although scientific in content, these definitions are purely regulatory in impact. Especially in the case of the USDA and EPA, these definitions determine the scope of regulation under existing statutes. Defining the scope of the statutory authority is properly the function of the agency charged by Congress with the administration of the statute.

The status of the BSCC's recommendations on these definitions and other matters of regulatory significance should be made clear. It would appear that unless and until they are adopted by the respective agencies in accordance with proper procedures, such definitions are merely suggestions. If any of the affected agencies chooses to modify the definitions, it would appear to be within their power.

There may exist theories under which the BSCC could claim some share in the regulatory authority of its member agencies. If the BSCC should somewhere find such authority, it would have to adhere to those procedures that are required of federal agencies engaged in rulemaking.

B. The Regulatory Sequence Exemptions

Turning to the substance of the regulatory sequence definitions, ELI is concerned about the exemption of so-called "well-defined regulatory sequences." According to the definitions suggested by the BSCC, transfers of regulatory sequences like promoters and terminators are exempt from categories of experiments that receive high-level review by regulatory agencies. The exemptions occur within a scheme that defines two categories of experiments as being of particular concern. These categories involve: 1) organisms that are engineered with genetic material from organisms more than a genera apart and 2) organisms that are or have received genetic material from pathogens. Transfers involving well-defined regulatory sequences are exempt from these categories because they do not present the dangers that led to the concerns about the categories. Put another way, transfer of regulatory sequences is not likely to convey pathogenicity to a non-pathogenic recipient nor to confer on a product organism the hybrid traits that would result from the combination of structural genes from dissimilar parents.

But this rationale does not support the conclusion that all transfers of regulatory sequences should be exempt. The major concern about engineered organisms is their novelty. The manipulation of regulatory elements—start and stop signals and modulators of the rate at which genes are synthesized—could conceivably introduce a significant degree of novelty that is independent of dissimilarity of gene products or pathogenicity. Even though the genetic engineer in such circumstances is confined to the same set of structural genes, he can use the regulatory elements to turn those genes on and off in different sequences, and to produce gene products in different amounts and in combinations with other gene products. The result could be an organism with a high degree of novelty. Rather than exempt such experiments from regulatory categories, consideration should be given to establishing a new category of regulatory manipulation that, along with pathogenicity, would receive high-level review whether transfers of genetic material are from inter- or intrageneric sources. In any case, this important issue needs greater public discussion by knowledgeable scientists.

Another point about the exemptions needs clarification. According to the definitions, the exemptions are allowed where investigators "can" show that the regulatory sequences are well characterized. Does this mean that an investigator must provide such information to substantiate the exemption to the relevant agency? That he must keep the substantiating data on file? Or merely that he must be confident that he could obtain the substantiating data, if he were asked. The decision about whether the sequences are well characterized should be made by the agencies rather than the investigators.

II. REGULATION OF AGRICULTURAL BIOTECHNOLOGY BY THE USDA

The second major topic is the regulatory program proposed by the USDA, particularly the regulatory arm of USDA, the Animal and Plant Health Inspection Service (APHIS). I would like to begin by noting that of the agencies faced with developing a biotechnology program, the Department of Agriculture has had by far the most difficult task. Unlike EPA or FDA, USDA administers a diffuse group of statutes that generally does not limit USDA to particular products, applications or activities. As a result, USDA was required to develop a comprehensive policy covering all agricultural applications of plants, animals and microbes in academic research, commercial research and development, and commercial use. This was a broad charge and the USDA policy evidences a lot of hard work toward meeting it. But the USDA regulatory policy falls short in several major respects. These deficiencies concern scope of coverage, quality of review, coordination within the agency, and statutory mandate.

A. Coverage

USDA has asserted jurisdiction over all agricultural applications of biotechnology and is the only agency asserting jurisdiction over plants and animals. The USDA is proposing that different activities be regulated under two different branches of USDA—the research arm, Science and Education, and the regulatory arm, APHIS. In general the USDA research arm will regulate USDA-funded research and will establish guidelines that will be offered for use by industry on a voluntary basis, as well as opportunities for review of products by the Agricultural Biotechnology Recombinant DNA Advisory Board (ABRAC). Under its regulatory arm, USDA intends to review organisms under the Virus-Serum-Toxin Act (VSTA) and the Plant Pest Act, both narrowly construed.

Although individual elements of the USDA scheme, particularly the research guidelines, have promise, the overall policy is unsatisfactory. Most importantly, the approaches taken by the two arms within USDA are totally inconsistent in their view of environmental risk and are badly in need of integration. The policy statements contain no guidance telling companies precisely when their projects would fall under the comprehensive, albeit voluntary, restrictions of the ABRAC guidelines or under the almost non-existent regulatory scheme of APHIS. In many cases both kinds of reviews appear to be required. This dual review seems duplicative and unnecessary and itself creates a host of procedural issues. It is not clear, for example, if one arm of USDA could, in the appropriate case, defer to the other and decline to review a product.

Overall the USDA scheme appears for the most part to leave the commercial research and use of products of agricultural biotechnology unregulated, except insofar as companies voluntarily choose to submit products or experiments to USDA's ABRAC. In the two instances where an enforceable regulatory regime will be imposed—the VSTA and the Plant Pest Act—the reviews contemplated appear not to be addressed to the scientific issues that have precipitated the interest in genetic engineering.

1. VSTA

Let me begin with the Virus-Serum-Toxin Act (VSTA). For the narrow categories of products it covers, the VSTA provides adequate prerelease review authority. Inexplicably, however, the policy statement does not make clear that engineered organisms reviewed under the statute will be reviewed for ecological safety. It is possible to infer such a review from statements made about NEPA, but nowhere are the protocols or test requirements for such a review described.

2. Plant Pest Act

a. Scope of regulation.

Besides the VSTA, USDA intends to assert enforceable authority over only one category of organisms—plant pests as defined under the Plant Pest Act. This definition includes, among other organisms, mites, nematodes, insects and other invertebrates but covers these organisms only if they are plant pests. It does not include them if they are beneficial to plants. The statute does not cover, regardless of their impact on plants or anything else, non-parasitic plants, i.e. most of the plant world, or vertebrate animals—including fish, frogs, poultry, and livestock.

In USDA's opinion, organisms that are not plant pests simply do not need to be regulated. I quote from the policy statement. "Other genetically-engineered organisms, which are engineered from certain organisms which are not plant pests or classified in taxa which do not contain plant pests need not be regulated."

This is a remarkable statement. Apparently APHIS believes as a scientific matter that only those genetically-engineered organisms that are plant pests pose a threat to the environment. If so, APHIS' position is at odds with that of much of the scientific community. It is also a position totally inconsistent with the USDA's ABRAC research policy which describes list upon list of organisms that need regulatory oversight.

It should be noted that APHIS' position is not the reluctant result of the limitations on its jurisdiction imposed by the Plant Pest Act. APHIS is not chafing at the bit of that jurisdiction. It appears to have embraced those restrictions as the lines along which a scientifically defensible policy can be developed. Scientifically, the policy totally misses the mark. As the ABRAC guidelines demonstrate, there are numerous organisms outside the confines of the plant pest category that are of concern and should be reviewed for environmental impact prior to review.

b. Quality of the review under the Pest Act.

Even where the USDA is asserting its regulatory authority, the reviews it intends to perform are going to be perfunctory and inadequate to address issues of ecological safety. According to its Federal Register notice, the review performed under the Plant Pest Act is aimed at determining whether an engineered organism is a plant pest. In that document, the USDA estimates that the information required to obtain a permit will cost only $5,000 to prepare and will not require the generation of any new data. The required information will include, among other things, descriptive data, country of origin, and quantities of planned introductions. None of the information on competitiveness or survival needed by other agencies is asked for by USDA. Although the notice claims that the information is supposed to be sufficient to allow USDA to assess the behavior of organisms in the environment, it is scientifically impossible to understand how USDA could make an assessment of ecological hazard without requiring additional case-specific data. The review contemplated by APHIS probably will allow the agency to make a determination of whether a plant is likely to be a plant pest but, in most cases, that determination would be a waste of $5,000.

The objective of the regulatory scheme is simply irrelevant to the mainstream scientific concerns about genetic engineering. Plant pests are part, but only a small part of the problem. Restricting the movement of, inspecting, and the careful packaging of plant pests in no way addresses the real problem. Moreover, other than herbicides, it would not seem likely that many plant pests are going to be intentionally produced. Of much greater concern are the organisms that are intended to do something beneficial, and are therefore planned for release in large numbers into the environment. Under this approach, these organisms will not be reviewed nor regulated at all.

Note further that the permits are required 180 days prior to "the time a person seeks to introduce a regulated article," but that critical term "introduce" is not precisely defined.

Lack of Mandate to Protect the Environment

The APHIS approach raises many questions about USDA's ability to protect broad environmental interests in the area of genetic engineering. As the USDA (APHIS) policy statement makes explicit, "USDA's mandate is to protect and enhance agriculture and forestry in the United States." APHIS' narrow approach to the regulation of biotechnology is fully consistent with this view of its mandate, but an adequate response to release of genetically engineered organisms demands a concern for the total environment, not just for the agroecosystem.

USDA's caution with regard to its mandate is justified. Congress has not charged USDA with protecting broad environmental interests. If it were to have stepped out boldly to protect the environment, USDA would have had nothing to stand on except for the National Environmental Policy Act and that would have proved to be a thin basis for a strong regulatory program. This lack of a mandate is the source of a gaping hole in the current biotechnology framework. EPA has such a mandate and is the better choice for the agency to regulate the broad environmental impacts of the agricultural applications of biotechnology. But if Congress wants USDA to take on this task, new legislation mandating the protection of environmental as well as agricultural interests will be needed.

Uncertainty of the Risk

One final general point about the framework document.

It disturbs me that the biotechnology policy pays very little attention to what appears to many to be the central feature of the deliberate release issue: its scientific uncertainty. Scientists have not yet determined whether or not the release of engineered organisms represents a serious economic and ecological threat. In the absence of data, plausible scientific cases can be made to support both positions. If the federal government chooses to control the technology at this early stage before its risks are fully understood, it must also attempt to resolve the uncertainty about the nature of those risks. The answers to the scientific question will not automatically fall out of the process of regulation. Understanding the nature of ecological risk must be made a regulatory goal that is specifically articulated and adequately funded.

Mr. VOLKMER. Thank you very much.
Dr. Riley.

STATEMENT OF DR. MONICA RILEY, PROFESSOR OF BIOCHEMISTRY, STATE UNIVERSITY OF NEW YORK AT STONY BROOK, AND AMERICAN SOCIETY FOR MICROBIOLOGY, AND CHAIRMAN, COMMITTEE ON GENETIC AND MOLECULAR MICROBIOLOGY OF THE PUBLIC AND SCIENTIFIC AFFAIRS BOARD

Dr. RILEY. My name is Monica Riley. To set the record straight, I am here to represent the American Society of Microbiology and not my home institution of the State University of New York. On behalf of the ASM I thank you for inviting the Society to present its views at this hearing. Our statement today is in the form of answers to the questions that you posed.

The first question has to do with definitions of the phrases "release into the environment" and "containment facility." The ASM does not at the present time endorse a particular definition of "release into the environment" or "containment facility." We are aware that the NIH/RAC is currently reviewing this issue, and we await their deliberations.

Meanwhile, however, we do have some observations on aspects of these definitions which cause us concern.

The word "release" implies to some an indiscriminate activity, sort of throwing things to the wind, so to speak. However, historically, microorganisms that are intentionally introduced into the environment are done so after a set of well-established stepwise procedures. It is routine to proceed from tests performed in the research laboratory to a greenhouse and thence to a small-scale isolated field plot, with provision for measuring effectiveness, survival, and spread of the microorganisms.

Therefore, we believe that the process of release into the environment or, perhaps better, "introduction into the environment" is not an indiscriminate process, but will occur only when the results of studies performed under controlled conditions indicate that a microorganism will pose little or no risk and can be used with confidence in the field.

There are two parts to the next question, which involves the existing statutory authority and regulatory policies. The first part: Do existing statutes provide sufficient authority for regulating introductions of genetically altered organisms into the environment? In our opinion, the June 26 version of the proposed new Federal guidelines for regulation are greatly improved over the December 1984 version.

The only reservation we have concerns the authority and applicability of the Toxic Substances Control Act, TSCA. We have not been persuaded that TSCA is an appropriate vehicle for regulating the introduction of altered organisms. The definition of genetically altered microorganisms as "new chemicals" is strained. Existing procedures for the control of toxic chemicals do not apply easily to the control of living microorganisms. It appears that it will be necessary for a new set of rules to be developed in order to be able, appropriately, to regulate living microorganisms under TSCA.

The second part: Do the proposed regulatory policies reflect an appropriate balance of risks and benefits, in our view. The answer is, yes, in our view the recently published guidelines do strike a good balance between risks and benefits.

We differ, in fact, in only a few points with the definitions of organisms subject to scrutiny. First, we do not favor exemption of intergeneric hybrids that contain only regulatory sequences in the introduced DNA. It is a little difficult to tell from the new guidelines just what level of scrutiny is specified for this particular class of intergeneric hybrids.

But we believe that there should be no distinction made between the level of review afforded to noncoding and to coding sequences. The reason for this is: Although in most cases regulatory—a foreign regulatory sequence will be entirely innocuous, still one must take into account the fact that some regulatory sequences have the capability to increase the expression of the associated gene very manyfold. Also, regulatory sequences carry specificity determinants which govern when a gene is turned "on" and "off" in response to chemically specific signals.

Although it is true that regulatory sequences do not effect the composition of the gene product in any way, there is the possibility of major quantitative changes in the amount of gene product produced and changes in the signal which would turn the gene "on" that could possibly in some cases cause problems.

Second, we suggest on the topic of the interaction of the microorganism and the environment, we suggest to further reduce risk, that more detail concerning the characteristics of the target environment be sought from the investigator at early stages of information gathering. It is the relationship between a genetically altered organism and a designated environment that determines the element of risk or safety of a combination of the two. Therefore, a description of the intended environment is of primary importance.

The next topic is the adequacy of the definitions of organisms to be examined for possible regulation, as stipulated in the preamble. The definitions used in the preamble to the Federal policy statement do include all organisms that we believe need to come under scrutiny for possible regulation, with the exception that is mentioned earlier. We prefer not to exclude from scrutiny the class of organisms that have incorporated extragenic regulatory sequences. We can add to this that we would favor excluding those intergeneric hybrids that are known already to exchange DNA in nature.

Concerning simple mutants with no genetic exchange, we make a distinction between nonpathogens and pathogens. First of all, concerning simple mutants of nonpathogens. We support the proposal in the guidelines to exempt them from regulation. With respect to deletion mutants, we recognize that only rarely, if ever, does the loss of a function have a harmful effect in a microorganism that is not classified as a member of a family of pathogens.

But as far as pathogens go, in contrast, we support the proposal that all pathogens and their derivatives, no matter what the alteration, should be scrutinized before being introduced into the environment.

It might be helpful at this point to dwell on the reason why we emphasize the difference between pathogens and nonpathogens. It is because these are not interchangeable categories. It is not a simple matter to generate pathogen from a nonpathogen. Pathogenic microorganism are those that cause disease in a host organism, whether the host be human, animal, or plant.

This requires an interaction between a pathogenic organism and a susceptible individual. There are many factors that are necessary for the expression of pathogenicity. There is communicability, transmissibility, invasiveness, infectivity, and virulence, each of these factors being highly polygenic properties. In other words, they are influenced or created or controlled by many different genes. Therefore, one cannot convert, by any simple genetic means, a nonpathogen to a pathogen because it requires the interaction of a great many genes to have an organism assume the function of a pathogen.

Quoting from the book "Microbiology," third edition, "The insertion of a gene for a virulence factor into a distantly related nonpathogenic microbe cannot be expected to convert it into a well-adapted effective pathogen." Therefore, we see these two classes of organisms as being quite different in the degree of care needed to be exercised.

In summary, the answer to this question, with the exception of the exemption of intergeneric regulatory sequences, we support the formulations of categories of organisms deemed to pose sufficient risk to warrant being scrutinized for the need of regulation before their deployment.

We have two short questions remaining. The next one: We were asked to provide examples in which alterations involving deletions of genetic material have significantly changed the interaction between an organism and its environment. The loss of function of a single gene in a nonpathogen can be debilitating to that organism and can prevent its being able to cope with a given environment. Only rarely does loss of a function result in a positive change, but there are such cases. Among pathogens, for instance, there is a case where a pathogen can change its host range as a result of simple mutation to loss of function. We are not aware of any comparable example of change in interaction with the environment in the case of nonpathogenic bacteria. So once again we make the distinction between those two categories.

Last, there is the question: Should all organisms contemplated for environmental release be reviewed on a case-by-case basis or should certain categories be exempted from review? There are certain categories that we favor exempting from scrutiny, at the outset, such as indigenous, nonpathogenic, intrageneric mutants, plus such intergeneric hybrids as are known to exist already in nature.

Otherwise, each case should be examined on its own merits and relevant existing knowledge be brought to bear along with new information provided by the interested investigator. The results of many such individual case studies, as in the operation of the RAC in the NIH, will accumulate in a growing database that will allow generalizations to emerge to guide the regulatory process, generalizations where a category of organisms together with a certain environment and a certain host spectrum could be exempted from review in the future, and other categories would be flagged for regulatory control as a class.

In conclusion, we view the current interest in biotechnology as reminiscent of the original debate 10 years ago concerning regulation of recombinant DNA. The NIH established the RAC committee, and their mode of operation has indeed been successful and so far no harm has resulted from recombinant DNA work. We believe that this—we should learn from that process, which has been used successfully in that context and could formulate oversight mechanisms so that each agency would establish flexible requirements which can be modified and relaxed as circumstances warrant and experience dictates. It can start on the conservative end and then as a lack of danger is demonstrated, can begin to be modified to introduce exempt classes.

Thank you very much for this opportunity to express the views of the ASM, and I would be happy to answer any questions you might have.

[The prepared statement of Dr. Riley follows:]

TESTIMONY

of the

American Society for Microbiology

presented by

Monica Riley, Ph.D., State University of New York, Stony Brook

before the

House Subcommittee on Investigations and Oversight,

House Subcommittee on Natural Resources,
Agriculture Research and Evironment, and the

House Subcommittee on Science, Research and Technology

of the

House Committee on Science and Technology

Hearing on

"The Coordinated Framework for the Regulation of Biotechnology"

July 23, 1986

Mr. Chairmen and Members of the subcommittees:

My name is Monica Riley and I am Chairman of the Committee on Genetic and Molecular Microbiology of the Public and Scientific Affairs Board (PSAB) of the American Society for Microbiology (ASM). On behalf of the ASM, I thank you for inviting the Society to present its views at this hearing to examine the new policy statements and guidelines of each federal agency that will regulate the products of biotechnology. The ASM is the largest single biological life science organization in the world, with an active membership of over 34,000. A committee of experts within the ASM consisting of members experienced in molecular biology and genetics, environmental microbiology, microbial physiology, and agricultural and industrial microbiology, was convened to develop a response to the six questions related to the new regulatory policies for biotechnology which are included in you letter of invitation. A consensus of that committee forms the basis for our statement today which is in the form of answers to the questions you posed. In addition to these comments, the ASM will be responding formally to the Office of Science and Technology Policy's Federal Register notice of June 26 concerning various aspects of the "Coordinated Framework for Regulation of Biotechnology."

I. Definitions of the phrases "release into the environment" and "containment facility"

The ASM does not at the present time endorse a definition of "release into the environment" and "containment facility." We are aware that the National Institutes of Health Recombinant DNA Advisory Committee (RAC) is currently reviewing the issue of defining deliberate release and several members of the ASM are participating in the review. We are looking forward to their conclusions and will review them independently. Meanwhile, we do have some observations on aspects of these definitions which cause us concern.

The term "release" implies to some indiscriminate activity. Historically, microorganisms are intentionally introduced into the environment through well established procedures. These procedures are followed regularly in waste treatment and in the agricultural industries. Prior to release into the environment, it is routine to proceed with tests performed in the research laboratory, to a greenhouse and then to a small-scale, isolated field plot designed to minimize the chance of dispersal and with provision for measuring the effectiveness of the microorganism intended for release, and for monitoring its survival and its spread or both.

We, therefore, believe that "release into the environment" will occur only when the results of studies performed under controlled conditions indicate that a microorganism will pose little or no risk and can be used with confidence in the field where conditions are not subject to complete control. According to our view, spraying a suspension of microorganisms on field plants or inoculating plants or animals that then have access to the outdoors constitutes release. A "containment facility" is a laboratory, greenhouse or other chamber in which microorganisms are confined and can be monitored under controlled conditions.

II. Statutory authority and existing regulatory policies of existing federal agencies involved in the review of biotechnology research and products

a. Do existing statutes provide sufficient authority for regulating introductions of genetically altered organisms into the environment?

The federal policy statements for biotechnology published in the June 26 Federal Register seek to regulate the introductions of genetically altered organisms into the environment by using existing regulatory powers under existing statutes. The proposed new federal guidelines for regulation are greatly improved in our opinion over the December 1984 version. The guidelines are impressive in their comprehensiveness and detail, and generally they are logical and consistent. The only reservation we have concerns the authority and applicability of the Toxic Substances Control Act (TSCA) which we understand would be used for certain industrial and environmental applications of genetically engineered microorganisms not covered by other statutes. We have not been persuaded that TSCA is an appropriate vehicle for regulating the introduction of genetically altered microorganisms into the open environment. We think the definition of genetically altered microorganisms as "new chemicals" is strained. Since existing TSCA rules and regulations are written for application to nonliving toxic chemical compounds, existing procedures do not apply easily to microorganisms. It may be necessary for new sets of rules and application formats to be developed in order to be able appropriately to regulate living microorganisms under TSCA.

b. Do the regulatory policies for the federal agencies as described in the federal policy statement reflect an appropriate balance of risks and benefits?

In general, we believe the new regulatory guidelines strike a good balance between risks and benefits. In line with past experience, the emphasis is on regulation of the groups likely to pose risk cases: nonindigenous organisms, pathogens and their derivatives, and intergeneric recombinants. Intrageneric constructs have been exempted from formal regulation. We agree in broad terms that the line has been drawn so as to provide a good risk/benefit ratio. We differ from the details of the guidelines on only a few points:

1) We do not favor exemption of intergeneric hybrids that contain only regulatory genes in introduced DNA. We are aware that introduction of foreign regulatory sequences in order to regulate specifically a gene of interest will in most cases be entirely innocuous. Nevertheless, we favor not making a distinction between coding and noncoding sequences. Strain construction that places a strong, effective regulatory sequence in a position of control over any particular gene can increase the expression of that gene many fold. This can influence rates of synthesis of key structural proteins that may affect a microorganism's capacity to compete and survive in natural environments.

Regulatory sequences also carry specificity determinants. A regulatory sequence can turn a gene on or off in response to chemically specific signals. Changing the signals to which a gene responds can constitute a substantial change in the biology of the recombinant organism with respect to that gene product.

Major quantitative changes in the production of a genetically determined substance could cause problems in some circumstances that do not exist when the substance is produced at low level. Take one hypothetical example: under normal circumstances a particular toxin might be produced by a bacterium at a rate that can be accommodated by a certain host organism, but if the toxin production were increased a hundred or a thousand fold, the host defenses could be overwhelmed. In this case, we hold that one would want to have the chance to gather information and to think about the likely consequences of, for instance, increasing the toxic level.

2) To further reduce risks, we suggest that more detail concerning the characteristics of the target environment be sought from the investigator at early stages of information gathering, together with data on its stability or

propensity to change (e.g. wet/dry, hot/cold, pH). The permits or licenses that are issued should apply only to the designated microorganism, and only to the type of environment that was explored in the preliminary testing protocols.

III. Adequacy of the definitions of genetic constructions to be examined for possible regulation as stipulated in the Preamble to the federal policy statements

The definitions used in the Preamble to the federal policy statements include all organisms that we believe need to come under scrutiny for possible regulation, except that, as mentioned earlier, we prefer not to exclude from scrutiny the class of organisms that have incorporated extrageneric regulatory sequences.

We would favor excluding from regulation that class of intergeneric hybrids that exchange DNA in nature by known physiological processes, in the belief that natural hybrids already exist in the environment.

In addition, we support the proposal to exempt from regulation simple mutants of nonpathogenic bacteria, including deletion mutants, and intrageneric recombinants. (By exclusion we do not mean exemption from established regulatory processes for products to be introduced into commerce.) With respect to deletions, we recognize that only rarely if ever does the loss of a function have a harmful effect in a microorganism that is not classified as a member of a family of pathogens. With respect to altered genes and intrageneric recombinants, we are not aware of any case in which a microorganism from a nonpathogenic genus has gained the unique physiology, invasiveness and toxicity required of a pathogen by simple mutation or by exchanging genetic material from within its genus.

We support the proposal that all pathogens and their derivatives, whether deletions, intrageneric recombinants or intergeneric recombinants, should be scrutinized closely before introduction to the environment. Pathogens have the capacity to mutate by single changes to increase in virulence or change in host range. Avirulent derivatives of pathogens have the potential to mutate to regain pathogenicity. Changes of these kinds have potential for harm.

It may be helpful at this point to illustrate how complex it would be to generate a pathogen from a nonpathogen. Pathogenic microorganisms are those that cause disease in a host organism, whether human, animal or plant. Practically no pathogen always causes disease -- in fact some may damage only a small proportion of hosts they infect. On the other hand, not every individual host is equally susceptible. Normally, healthy humans, animals or plants are susceptible to a specific range of organisms. Bacteria cause disease mainly by three basic mechanisms: invasion of tissues or surfaces, production of potent toxins, or by invoking hypersensitivity reactions. To be naturally pathogenic, a microbe must be communicable to a susceptible individual. The virulence of the microorganism is a function of the efficiency of its infectivity and invasiveness (including the ability to colonize target tissues) and of the severity of the disease produced. The factors of transmissability, invasiveness, infectivity, and virulence are highly polygenic properties of pathogenic bacteria (i.e. they are influenced or controlled by many different genes). As presented in the textbook Microbiology, Third edition, by B.D. Davis, R. Dulbecco, H.S. Eisen, and H.S. Ginsberg, "the adaptation of a microorganism to its ecologic niche depends on the evolution of a balanced genome. Hence the the insertion of the gene for a virulence factor into a distantly related nonpathogenic microbe cannot be expected to convert it into a well-adapted, effective pathogen."

Continuing with the definition of genetic constructs that should be examined for possible regulation, we agree with the stipulation in the Preamble to the federal policy statements that all nonindigenous organisms should be examined carefully before introduction into the open environment. Many examples are known of deleterious consequences following an introduction of nonindigenous organisms into environments that may be deficient in natural predators. We recognize that significant risk may lie in this category.

In summary, with the exception of the exemption of intergeneric regulatory sequences, we support the formulations of categories of organisms deemed to pose sufficient risk to warrant being scrutinized for need of regulation before their deployment.

IV. Examples in which alterations involving deletions of genetic material have significantly changed interaction between an organism and the environment

Loss of function of a single gene in a nonpathogen can destroy the ability of the strain to grow or survive under specified nutrient or environmental conditions. Loss of a single function can convert an organism from antibiotic resistant to antibiotic sensitive. Loss of a single genetic and biochemical function can be debilitating to the organism.

Only rarely does loss of function result in a positive change, but such cases do exist. A pathogen may change its host range as a result of mutation. We are aware of an instance of a microorganism that is pathogenic to certain plants which, as a result of mutation to loss of a single function, gained infectivity for one plant and simultaneously lost infectivity for nine other plants. We are not aware of a comparable example of change in interaction with the environment in the case of nonpathogenic bacteria.

V. Should all organisms contemplated for environmental release be reviewed on a case-by-case basis, or should certain examples or categories be exempted from review?

As mentioned above, there are certain categories that we favor exempting from scrutiny at the outset, such as indigenous, nonpathogenic, intrageneric mutants and such intergeneric hybrids that are known to exist already in nature. These classes aside, all other cases could be scrutinized individually. At the start, we would expect each case of an organism designed for introduction into the environment would be examined on its own merits, bringing all relevant information to bear in evaluating the case. Relevant existing knowledge will be applied to the case and new information will be gathered by the investigators in their preliminary trials. The preliminary experiments will reveal what environmental factors are important to the survival and growth of an organism in question under the specified environmental conditions and what factors are important to optimize and control expression of the particular gene of interest.

The results of such individual case studies will accumulate in a growing database containing information about the physiological characteristics of various organisms, their survival, growth, and their interaction with other organisms, all as a function of environmental parameters. As such a database develops, some categories of microorganisms in relation to some categories of environments will be found to constitute no threat and these combinations may at that time be judged as exempted from regulation. Other categories of combinations of organism and environment will be found to pose a risk, and these categories will be flagged for regulatory control as a class. In due course, with accumulated data and experience, generalizations will emerge to guide the regulatory process, and case-by-case treatment will wane.

In conclusion, we view the current interest in biotechnology as reminiscent of the original debate 10 years ago concerning regulation of recombinant DNA research. Based on the concerns of the American Society for Microbiology, along with other scientific societies, government agencies and the Congress, the National Institutes of Health (NIH) established the Recombinant DNA Advisory Committee (RAC). Since RAC's inception there have been no laboratory manipulations or accidents which have caused harm to workers or the environment. We strongly urge that regulations be considered in the context of the extensive experience that has been gained by the successful operation of the NIH RAC. We should learn from the process used in regulating recombinant DNA research in which the original guidelines were overly cautious and conservative but were deliberately designed to be relaxed quickly as new information permitted. We believe that in formulating oversight mechanisms, each agency must establish flexible requirements which can be modified and relaxed as circumstances warrant and experience dictates.

Thank you very much for this opportunity to express the views of the ASM. I would be happy to respond to any questions that my presentation may have raised.

Brief Biographical Sketch of Monica Riley, Ph.D.

Ph.D, University of California at Berkeley, 1960
Assistant Professor of Bacteriology, University of California at Davis, 1960-66

Associate Professor of Biochemistry, State University of New York, Stony Brook, 1966-75, Professor, 1975 to present.

Visiting Scientist at Stanford University School of Medicine, 1961, Harvard University Department of Biological Sciences, 1965, and University of Brussels, Belgium, 1981.

Provost of Biological Sciences, State University of New York, Stony Brook, 1975-78.

Research in areas of bacterial conjugation and recombination, physical chemistry of nucleic acids, evolution of bacterial genes, nucleotide sequences of coding and non-coding regions of bacterial DNA.

Served on Commission on the Future of Life Sciences at State University at Stony Brook, 1985.

Chairman of Institutional Biosafety Committee, 1985-present.

Member of Editorial Advisory Board for Volume III of _Bacteria in Nature/ A Treatise on the Interactions of Bacteria and Their Habitats_, ed. by J.S. Poindexter and E.R. Leadbetter, Plenum Press.

Mr. VOLKMER. Thank you very much, Dr. Riley.

We will now proceed to the testimony of Dr. Norse.

STATEMENT OF ELLIOTT A. NORSE, PH.D., DIRECTOR, PUBLIC AFFAIRS OFFICE, THE ECOLOGICAL SOCIETY OF AMERICA

Dr. NORSE. Ladies and gentlemen, I am an ecologist, and I represent the Nation's ecologists in the Public Affairs Office of the Ecological Society of America [ESA].

Because ecology is so important to understanding the relationship to people and environment, the media and the general public often equate ecology with environmentalism, but we're not an environmental organization. We are a scientific professional society of about 6,500 people in every State, in 65 nations around the world, who study the interactions of plants, animals, and microorganisms in their environment.

Ecologists have no special expertise in the actual engineering of plants, animal, and microbial genes. That is largely the province of molecular biologists. Rather, our science gives special insights into two crucial questions: What modifications of organisms can serve human needs, and what happens when modified organisms are released into the environment?

Like our colleagues in molecular biology, we see great potential for genetic engineering; cleaning up pollution, and agriculture, et cetera, and we are dismayed by the work of some nonscientists who hamper research and commercialization of genetically engineered organisms.

But we tend to differ from molecular biologists about the risks involved. Molecular biologists who develop the new techniques are understandably eager to see them used widely. Opportunities for employment and profit also spark their enthusiasm. In contrast, very few ecologists are employed in designing new organisms or in assessing the consequences of their release, although that could change.

Nonetheless, the differences between molecular biology and ecology go a lot deeper. Molecular biologists explore the mysteries of the invisible world within cells in clean, orderly laboratories. We explore the mysteries of nature in fields, forests, and wetlands. Rather than working with the smallest, most isolated components of life in controlled situations, we examine the interactions of living things in the fascinating, messy, enormously more complex world outside. The interactive processes of nature is our specialty.

A century of research has taught us one lesson: When novel organisms are introduced into environments, they may disappear without a trace, or they may pose serious problems.

As a result, we find ourselves in the middle between the uninhibited enthusiasm of the industry and the unyielding opposition of some nonscientists. But we also find that the scientists who have so far dominated the discussion of biotechnology don't understand the interactions of living things in their environments well enough to justify their assertions that the risks are insignificant. Consequently, our enthusiasm about genetic engineering is tempered with caution.

The coordinated framework seeks to do something very difficult: to create consistency in regulating diverse engineered organisms by diverse agencies. Unfortunately, I believe that the preamble is questionable in both science and policy because it leans too far toward allowing releases without appropriate safeguards.

The preamble seems to reflect the views of genetic engineers, not those of ecologists. Although the BSCC recently stated that it sought input from scientific societies, it never contacted ESA. Given the central role of ecology in this issue, that seems to be a serious omission. Unfortunately, the framework clearly reflects the absence of our input.

I disagree with the criteria by which the BSCC exempts organisms from rigorous review. There is good reason that we exempt some organisms. Government shouldn't inhibit industrial processes known to be safe. But the decision to focus on pathogens and organisms having intergeneric combinations suggests a serious misunderstanding of taxonomy and ecology. Taxonomists have varying ideas of what constitute a species, genus, or higher taxon. Those working on mammals on the one hand and bacteria on the other see things very differently. Taxonomists consider, for example, chimpanzees and people to be so different that they put them not only in different genera but in different families. Yet 99 percent of the genes of chimpanzees are the same as ours. I suspect that chimps and people differ genetically much less than different species within bacterial genera such as *Pseudomonas, Bacillus,* and *Clostridium.*

The intergeneric criterion reflects inadequate understanding of variations among species in a genus, and these differences can be crucial. Two examples: Potatoes are an important food plant in the genus Solanum, but you would do well to avoid eating the Solanum called "deadly nightshade." Many species of *Bacillus* bacteria are harmless to humans and livestock; but one of them causes the deadly disease anthrax.

These are dramatic examples, but problems are more likely to arise when more subtly differing traits are transferred among species within a genus. Because so little is known about the ecology of most species, especially microorganisms, if we were to transfer genes between the *Pseudomonas* bacterium that inhabits leaves and a different pseudomonas that inhabits roots, we might alter the biochemical cycles that maintain soil fertility. Unless ecologists were to examine such situations carefully, important effects might go unnoticed by those charged with protecting the public. But the farmer saddled with growing fertilizer bills would be forced to pay for our negligence.

Unfortunately, there is currently no definitive way to predict what an organism will do when released into the environment, for two reasons. One is that genetic manipulations are imprecise to varying degrees. We just don't know precisely what the products are going to be. For another, nobody can predict with assurance the fate or effects of an organism released into the real world.

Vastly more is spent on molecular biology than ecology. The ability to produce the organisms has outstripped our ability to predict the consequences of their release. If the agencies that fund ecological research don't correct this, the gap is going to grow, and the

BSCC is in a unique position to eliminate the disparity and thereby decrease the uncertainties that currently inhibit progress in biotechnology.

Altering regulatory sequences amd deleting genes can affect an organisms' survival, reproduction, and have environmental effects. I surmise that the rationale for exempting these alterations is that if no sequences coding for proteins are modified, changes will be merely quantitative and, hence, minor.

Imagine, however, altering the genetic sequences of a house cat that governed the rate of production of growth hormone so that you obtain a puma-size kitty. Those who consider this far-fetched should recall that genetic engineers have already produced mice that are as large as rats. Anyone should understand that an organism as different as normal- and puma-size cats would differ not only quantitatively but also qualitatively in their effects on the environment.

And again I cite a dramatic example to emphasize a point that is likely to be much more subtle in practice and thus more likely to be overlooked by nonecologists. Regulatory sequences that change growth and reproductive rates by just a few percent could dramatically alter competitive balances among organisms in nature.

The preamble's focus on pathogens also reveals a poor understanding of ecology. If the aim is to avoid adverse environmental effects, we also need to examine organisms' other interactions, including predation, parasitism, competition, and mutualism. The focus on pathogens suggests that those who drafted the framework have the narrow view of life peculiar to those in human-centered biological disciplines: that either organisms are pathogens, or that they can safely be ignored. In fact, the species eliminated by a competitor, a predator, or a parasite is just as extinct as one eliminated by a pathogen. The input of ecologists would have helped the BSCC to appreciate this.

For now we lack hard data, so assessing risk must be more theoretical than empirical. The best we can do is extrapolate from what we know, use our scientific judgment and then hope for the best.

Under these circumstances, exempting any of the processes of altering genomes developed in the last 15 years seems premature. It seems prudent to regulate releases on a case-by-case basis. We need to gain experience to formulate rules that will not inhibit research, development, or commercialization of products, but that will protect us from the unanticipated effects that always crop up with new technologies.

I know that investors and molecular biologists are eager to proceed, but I also know that the public will not be happy if something goes awry. Challenger, Chernobyl, and other failures of technology are too deeply embossed in their minds. At this stage it behooves us to proceed prudently.

As those involved in genetic engineering since the mid-1970's know well, we can always relax standards should experience show that intensive review or other safeguards prove unnecessary.

Thank you.

[The prepared statement of Dr. Norse follows:]

TESTIMONY OF ELLIOTT A. NORSE, Ph.D.

DIRECTOR, PUBLIC AFFAIRS OFFICE, THE ECOLOGICAL SOCIETY OF AMERICA

ON

THE COORDINATED FRAMEWORK FOR THE REGULATION OF BIOTECHNOLOGY

PRESENTED TO

U.S. HOUSE OF REPRESENTATIVES COMMITTEE ON SCIENCE AND TECHNOLOGY

SUBCOMMITTEES ON:

INVESTIGATIONS AND OVERSIGHT

NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

AND

SCIENCE, RESEARCH AND TECHNOLOGY

***

July 23, 1986

The Ecological Society of America
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Congressmen Scheuer, Walgren and Volkmer, Honored Committeemembers and Guests:

My name is Elliott A. Norse. I am an ecologist. I was trained at Brooklyn College, the University of Southern California, and the University of Iowa. Since 1983, I have represented the nation's ecologists as Director of the Public Affairs Office of The Ecological Society of America.

Because the science of ecology is so important to understanding the relationships of people and our environment, the media and the general public often equate ecology with environmentalism. However, The Ecological Society of America is not an environmental organization but a scientific professional society. Ecologists are scientists who study the interactions of living things and their environments. Some of us are specialists on the ecology of particular groups of plants, others specialize on animals, still others specialize on microorganisms. Ecology is a highly mathematical, increasingly experimental science. Among the 6,500 members I represent, nearly 2/3rds are Ph.D.s. Many of the remainder are Ph.D. candidates. Ecologists do research, teach and participate in decisionmaking in universities, state and federal agencies, industry and environmental organizations. ESA members live and work in every U.S. state and some 64 other countries.

Ecologists have no particular expertise in the actual engineering of plant, animal and microbial genes. Such genetic manipulation is largely the province of cell and molecular biologists. Rather, our science gives us special insights into two kinds of questions that are crucial in genetic engineering. One is "What modifications of organisms could serve human needs?" The other is "What happens when modified organisms are released into the environment?"

It is useful to consider a hypothetical example with three steps. As a first step, ecologists would identify the need for a bacterial pesticide that can be engineered to control gypsy moths. Second, molecular biologists would transfer genes from one bacterium that produces a toxin to another bacterium known to live harmlessly in the gut of gypsy moth larvae, so that after their ingestion, the modified gut bacteria would poison the larvae. And then third, ecologists would determine both the success of the new bacterium in doing what it was designed to do and the direct and indirect side-effects of releasing it into the environment.

The differing roles of ecologists and molecular biologists contribute to our differing perceptions about the risks of genetic engineering. The molecular biologists who develop these new techniques are understandably eager to see the products of their labors used widely. The exciting opportunities for employment and profit further spark their enthusiasm. Molecular biologists have lots of incentive. In contrast, few, if any ecologists are now employed in designing new organisms or in assessing the consequences of their release, although that could change in coming years. For now, we have considerably less incentive.

Nonetheless, the differences between molecular biologists and ecologists go much deeper than differing levels of incentive. Molecular biologists work in laboratories to penetrate the mysteries of the invisibly tiny world within cells. In contrast, for the most part, ecologists work in the fields and wetlands and forests to unravel the mysteries of nature at a vastly larger scale. We deal with species, ecosystems, the entire biosphere. Rather than working on the very smallest, most isolated components of life in situations far removed from nature, our work examines the interactions of living things in the fascinatingly complex world that we can see. The patterns and processes of living things in natural and managed ecosystems is our specialty. And we have learned an important lesson during more than a century of research: when novel organisms are introduced into the environment, the consequences can range from effectively nonexistent to very serious, very expensive and irreversible.

As a result of this knowledge, we tend to find ourselves in the middle, between the uninhibited enthusiasm of so many molecular biologists and the unyielding opposition of some nonscientists. We are excited about the promise of the new technologies to improve agriculture and lessen pollution. We understand that genetic engineering could become a powerful tool for conserving organisms in danger of extinction. We are dismayed by some of the ill-founded arguments advanced by nonscientists who would stop genetic engineering research, development and commercialization. But we are concerned that the scientists who have thus far dominated discussion of this issue have too little understanding of the interactions of living things in their environments to justify their confidence that the risks are insignificant. Consequently, our enthusiasm about genetic engineering is tempered with caution.

Although I heartily approve of the Administration's stated intention of creating consistency in the regulation of different kinds of engineered products by different agencies, I am disappointed by the Coordinated Framework for the Regulation of Biotechnology. I found that it is not particularly coordinated, that it is plagued by some serious conceptual problems, and that, as a result, it is unbalanced, leaning too far toward allowing releases of engineered organisms without the safeguards that are appropriate at this stage of the technology's development. Because of the size and complexity of the Framework, I will confine my comments to certain aspects of the preamble.

The preamble developed by the Biotechnology Science Coordinating Committee seems to reflect the views of molecular biologists and the biotechnology industry, not those of ecologists. Although the BSCC stated in its recent public meeting that in assembling this Framework it sought input from the scientific societies, BSCC never contacted The Ecological Society of America to learn of the ideas and opinions of ecologists. Given the central role of our science in the development of any sound regulatory framework, this is a serious omission. Unfortunately, the Framework clearly reflects the absence of our input.

The tilt toward minimizing safeguards begins with the first page of the Framework. BSCC states that the recent developments in biotechnology are an extension of traditional genetic manipulations, and that they are promising because "they enable more precise genetic modifications." This diverts attention from worrisome aspects of genetic engineering by emphasizing the precision of the techniques and ignoring their novelty. Although it is true that some genetic engineering might actually duplicate naturally occurring genomes, no amount of conventional genetic manipulation could have induced E.

coli bacteria to produce human insulin. It is the ability of the new techniques to transcend natural genetic processes and traditional genetic manipulation that creates essentially new kinds of organisms, thereby raising widespread concern. Informed observers also have reason for concern about genetic alterations that change organisms quantitatively (see discussion about growth hormones below).

The general public is poorly informed about science and fearful about new scientific and technological developments. As a result, nonscientists mistrust scientists. And while the media are often slow to provide the public with scientific data and theories essential to informed decisionmaking, they are quick to pick up any hint that scientists are misleading the public. Understating the power of new technologies does nothing to calm the public's fears, and hence does not advance the development of industry in the long run. It also runs counter to the recomendation by the OECD report on recombinant DNA that special efforts be made to improve public understanding. I must add that actions by some companies and a federal agency involved in genetic engineering have not helped to increase the public's trust.

I cannot agree with the criteria by which BSCC decided to exempt organisms from rigorous review before allowing their release into the environment. My objections are based on my understanding of both science and policy. There is good reason to exempt certain groups of organisms from the most rigorous regulatory analysis: we should not inhibit industrial processes we know to be safe. But the decision to limit rigorous agency review to pathogens or organisms having intergeneric combinations suggests serious inadequacies in BSCC's understanding of taxonomy and ecology.

Despite scientific attempts to make sense of the diversity of nature, the names we give to groups of organisms (taxa) are necessarily arbitrary assessments of our educated opinion about relationships. Unfortunately, taxonomists have varying ideas of what constitutes a species, a genus, or a higher taxon. A taxonomist who emphasizes diversity of organisms might see many species or genera where one who emphasizes the unity of life sees few. Taxonomists working on mammals and those working on bacteria tend to see things very differently. Taxonomists consider people and chimpanzees so different that they put them not only in different genera, but in different families. But molecular biologists have shown that 99% of the genes of chimpanzees are the same as those of humans. I suspect that chimpanzees and we differ genetically much less do than different species within bacterial genera such as Pseudomonas, Bacillus or Clostridium.

Even if a genus were to mean the same thing to a mammalian taxonomist and a bacterial taxonomist, the BSCC's intergeneric criterion would reflect inadequate understanding of the variation among species in a genus. These differences can be crucial to us. A few examples should suffice. Most species of sumac trees in the genus Rhus are quite harmless to people, but poison sumac is not. Potatoes and eggplants are important food plants in the genus Solanum, but you would do well to avoid eating the Solanum called deadly nightshade. Many species of Anopheles mosquitoes cannot host malarial parasites, but those that do carry the world's worst infectious disease. Many species of Bacillus bacteria are harmless to humans and livestock, but one of them causes deadly anthrax.

I am deliberately citing dramatic examples, but in practice, problems are more likely to arise when more subtly differing traits are transferred among species within the same genus, because science knows so little about the ecology of most species, especially microorganisms. If, say, we were to transfer genes between Pseudomonas bacteria that inhabit leaves and different Pseudomonas that inhabit roots, we might be altering the biogeochemical cycles that naturally maintain the fertility of soils. Unless ecologists examine such situations carefully, important effects might go unnoticed by those charged with protecting the public and the environment. But the farmers saddled with growing fertilizer bills would be forced to pay for our negligence.

I would urge responsible officials to change this criterion, at very minimum, to require higher levels of review for interspecific, rather than intergeneric transfers. This would by no means eliminate the problem; one can also cite examples of species, including microbial species, in which some genotypes are much more likely to produce undesirable effects than others. Similarly, we know that some species are opportunists that are not harmful under most circumstances, but can become problems when the species or ecosystems with which they are associated are stressed. At this early stage of regulation, prudence is warranted. As those involved in genetic engineering since the mid 1970s well know, we can always relax standards at a later date when experience shows that intensive review or other safeguards prove unnecessary.

In my view, requiring rigorous review only for interspecific transfers is still inadequate. Certain advocates of genetic engineering have two banners that they wave vigorously at meetings whenever the opportunity arises. One is "Regulate the product, not the process." Without commenting on the wisdom of this slogan, I must point out that the BSCC Framework, in exempting deletions of genes and transfers of genetic regulatory sequences, is emphasizing process over product.

Unfortunately, there is currently no definitive way to predict the product will be, that is, what an organism will do when modified and released into the environment, for two reasons. For one, because the genetic engineering processes are, to varying degrees, imprecise, we do not know precisely what the products will be. I think that, when pressed, the genetic engineers among us will admit that "well-characterized" does not necessarily mean that they know precisely the nature and function of all the genetic material that they are transferring or deleting. Without knowing the attributes of the new organisms in the context of the environments in which it will ultimately occur, I find the exemptions for transfers of ostensibly "well characterized" genetic material disturbing.

The other reason is that even if genetic engineers always knew precisely the nature and function of the genes they were transferring, it does not follow that they—or anyone else at this point--could then predict with sufficient assurance the fate and effects of the modified organism when it is released. The federal government and the private sector have spent and continue to spend vastly more on molecular biology and the technologies to develop new organisms than on ecology and the scientific techniques needed for predicting the consequences of organisms released into the environment. Regrettably, our predictive capability is not yet nearly sufficient, a reason that the previously mentioned OECD document recommended further research to improve prediction, evaluation and monitoring of the outcome of application of engineered organisms. If agencies that fund research do not take corrective action, the gap between the need for greater predictive capability and our ability to fulfill that need will inevitably grow.

Alteration of regulatory sequences and deletion of genes, which are exempted from intensive review under this Framework, can affect the characteristics of organisms in ways that affect their survival, reproduction and effects on ecological systems. I surmise (for it is not stated clearly) that BSCC's rationale is that if no sequences that code for proteins are modified, other changes will simply quantitative, and hence minor.

I am dismayed by this exclusion. Imagine altering the genetic sequences of a housecat that govern the rate of production of growth hormone to obtain a mountain lion-sized kitty (incidentally, both housecats and mountain lions are members of the genus Felis). Although this particular possibility has not cost me much sleep, those who consider it farfetched should recall that genetic engineers have already produced mice that grow as large as rats. Any biologist should be able to understand how organisms as different quantitatively as normal-sized and puma-sized cats would have not only quantitatively, but also qualitatively different effects on their environments.

Again, I cite a dramatic example to underline an important point that is likely to be more subtle in practice, and therefore more likely to be overlooked by nonecologists. Regulatory sequences that change growth or reproductive rates by just a few percent could dramatically alter competitive balances among microorganisms, plants or animals in nature. And although, during discussions about this issue in the last several year, I have heard biologists without training in ecology suggest that altering organisms will inevitably lower their abilities to survive and compete, ecologists would not have difficulty envisioning alterations that might increase the survival and reproductive fitness of organisms, and thereby change the composition and dynamics of natural or managed ecosystems.

Because these new technologies have not yet been tested legally in the U.S., and because the first permit applications only hint at the kinds of environmental releases we can expect in years to come, current assessments of risk must be more theoretical than empirical. The best we can do now is extrapolate from what we know, use our scientific judgment, and then hope for the best. Under these circumstances, exempting any of the processes of altering genomes that have developed in the last 10-15 years from rigorous review seems premature.

Until we know more, it seems prudent to observe the second oft-waved banner: regulating such releases on a "case by case" basis. We need to gain experience with environmental releases so that we can formulate empirically based rules which will not inhibit research, development and commercialization of products, but which will protect the environment from the unanticipated adverse effects that will inevitably crop up with these technologies (as they do with all new technologies). Lacking years of case-by-case studies and careful analyses by qualified scientists, the sweeping exemptions in BSCC's Framework are worrisome. Because the great majority of engineered organisms will probably be harmless but a very small fraction might have important adverse environmental consequences, and because we do not yet know enough to differentiate those posing trivial and major risks, a more sensible policy would be to learn all we can now, relaxing regulations as the facts and theory catch up with our actions. I know that investors and molecular biologists are very eager to proceed, but I also know that the public will not be happy if something goes awry. Challenger, Chernobyl and other failures of technology are too deeply embossed in their minds. It behooves us to proceed prudently.

The preamble's focus on pathogens again reveals a poor understanding of ecology. If our decisionmakers seek to avoid adverse environmental effects from releasing organisms, we need to examine not only the possibility that organisms might be pathogens, but also their other interactions with other species, including predation, parasitism, competition and mutualism. The focus on pathogens to the exclusion of other important kinds of species suggests that those who drafted the Framework have the narrow view of life peculiar to those in biomedicine and other human-centered biological subdisciplines--that either organisms are pathogens or they can safely be ignored. In truth, a plant or animal or microbe eliminated by a competitor or predator or (by the BSCC definition) non-pathogenic parasite is just as extinct as one eliminated by a pathogen. We also need to examine the effects of engineered organisms on the abiotic components of the environment, that is, on the biologically mediated cycles of chemical elements that determine the chemical composition of the water, soil and air and many physical characteristics of the biosphere. The web of interactions among species outside the ideal world of laboratory glassware is vastly more complex than the Framework implies. The input of ecologists would have helped BSCC to appreciate this.

Thank you for the opportunity to address your Subcommittees on this important topic.

Mr. **Volkmer**. Before I go to questioning of the witnesses, I would like to ask Dr. Kingsbury if he would like to make any comments on the testimony of any of the three witnesses that have testified.

Dr. **Kingsbury**. I think that it's probably not appropriate to make extensive comments. There is a cautionary note that I would like to—that I would like to throw out, and that is that there is a tendency to focus attention, by people who look at the framework, at the preamble. Now, I think that all of us in Washington who deal with these giant documents that come flowing across our desks have fallen into the trap of only reading the executive summary, only to discover that soon someone is asking us about something that was embedded in chapter 7 which we never managed to get to. I think that the same--the same principle applies here.

The executive summary of the statement was really an overview, and we have tried to caution people that to get the detailed and intricate information that really is part of the policies, one needs to read the policies from each of the agencies. I think that a reflection of that is the notion as to what is really involved in the review of microorganisms. As I pointed out earlier, the EPA document, in their summary table, very clearly lines out the fact that there are no classes of organisms, microorganisms, that are not reviewed; it's simply the nature of the review.

I think we must keep that kind of perspective as we go on to these discussions. There are not things that are completely out of the regulatory matrix, but it's a question of the regulatory approach that is—that is being taken.

All microorganisms are falling within the EPA review. With that, I think I will stop.

Mr. **Volkmer**. Dr. Kingsbury, I have reviewed the testimony of the three witnesses that we received earlier, and after I reviewed it, I have some questions in my own mind, being a non-scientist, about the definitions. Maybe you can understand that after listening to the testimony.

Dr. **Kingsbury**. Yes, sir.

Mr. **Volkmer**. As someone who is trying to remain objective in all this, I am wondering now which is right.

One of the things that does concern me, those again that are trying to provide some oversight for the Congress on the development of biotechnology regulation—is whether we really had say, full input from all facets that should have been involved in the development of that.

With that, I would like to ask you, as I understand it, on the BSCC—and we went over this once before in our earlier hearing—that you and Dr. Young both have Ph.D.'s in microbiology. Is that correct?

Dr. **Kingsbury**. Yes, sir.

Mr. **Volkmer**. Are there any other scientists on the BSCC?

Dr. **Kingsbury**. Dr. Wyngaarden has had a distinguished career in clinically related sciences. Dr. Bentley, prior to coming to the USDA, was a—you know, on the faculty of the University of Illinois as an agricultural scientist and then as an academic administrator, but he has certainly had some background.

I believe that Dr. Don Ehreth, who is the Acting Assistant Administrator for Research and Development at EPA, has a scientific background. I am not sure what that is; it's probably chemistry or toxicology.

Mr. VOLKMER. What bothers me a little bit, I guess, is what is bothering Dr. Norse. As one who sees the products that are going to come forward in the next years—and I say "years" because who knows how long before we develop something else—they are all going to impact on the environment.

No ecologists, is that correct, were involved in the development of the guidelines?

Dr. KINGSBURY. I think that that may be a bit of an oversimplification in the sense of the breadth of the process of agency review that went on. The agency positions were developed through broad discussions with their advisory committees, their committee structure. Agriculture brought in a wide variety of people who have helped them develop their policy. EPA has consulted widely with members of their Scientific Advisory Committee, which have heavy representation. In fact, if I am not mistaken, the Chair of the Scientific Advisory Committee is, in fact, an ecologist, Dr. Alexander, who appeared—I can't remember now which hearing he—which committee he was before, but it may have been this one—some time ago. So there have been in the agencies the involvement of microbiologists.

In terms of NSF's own personal activity, the chairman of the Biological, Behavioral and Social Sciences Advisory Committee is a—is not a microbial ecologist but a tropical biologist ecologist.

I believe that there is, at different levels of agency activity, representation of a variety of scientific specialties. Within the BSCC itself, you are absolutely right, there are no ecologists sitting on that committee. There are people who represent the ecological research environment, in the cases of Dr. Ehreth; certainly the R&D activity at the EPA is a reflection, to a great extent, of that kind of activity. Certainly, NSF is involved in that. I won't claim to represent the ecologists in that context, but certainly we have input from them.

So it's a question of agency-level participation versus coordinating committee participation.

Mr. VOLKMER. Well, then you're saying—well, let me put it this way. The definitions as to what should be subject to review and how much review, was determined by the BSCC?

Dr. KINGSBURY. No, not that—that's not strictly true. The BSCC, as was pointed out, has no statutory responsibility.

Mr. VOLKMER. That's right.

Dr. KINGSBURY. So it has no direct definitions that it applies to anything. It worked with the agencies, to assist the agencies in getting consistency within their definitions. The definitions that go into place are those in the agency statements. The agencies worked with their advisory committees as they derived what they believed were appropriate statements. They worked with the BSCC in the derivation of what is an appropriate common statement, so that there was consistency.

But the Environmental Protection Agency, I can assure you, is going to work through its advisory committee structure before it comes forward with a definition as important as the definition of a new organism.

Mr. VOLKMER. Just to go along with this type of question, because I have just been handed a note now that Dr. Alexander asked this committee for a copy of the guidelines in May, which we didn't have. He, as I understand it, had no input. I understand that he was on the AGS ice-minus review panel, but he had no input in establishing the guidelines and definitions.

Dr. KINGSBURY. That is an agency question that I can't answer; I am sorry.

Mr. VOLKMER. I will talk to Dr. Moore later when we have our next panel on that, and make a determination on that.

Just again to go on with background, can you give me the types of courses that you have had in ecology in your educational background?

Dr. KINGSBURY. Actually, when I was a graduate student at the University of Washington, I did my thesis work on microbial ecology in the Columbia River watershed.

Mr. VOLKMER. Have you ever had just ecology?

Dr. KINGSBURY. It's been a long time. [Laughter.]

I would venture to say at this point I do not remember taking a course called "Ecology."

Mr. VOLKMER. Or population ecology?

Dr. KINGSBURY. At the time that I was an undergraduate, those were not subject areas that were dealt with in that context. Microbial ecology certainly was, and as I said, I did that for my initial thesis work.

Mr. VOLKMER. Because basically you are in the microbial field.

Dr. KINGSBURY. I am a microbiologist.

Mr. VOLKMER. Right.

Dr. KINGSBURY. And we studied at the time a complex ecosystem in the Columbia River watershed that dealt with the epidemiology and ecology of a disease of salmonid fishes that had a complex environmental interaction. It was a disease that was a warm-water disease yet would winter over during very cold periods. So it was a classic case of an ecological intruder that was creating a problem, and that was the thesis work that I was involved in.

Mr. VOLKMER. Dr. Riley, was ASM, as an organization, to your knowledge, ever contacted officially or informally to provide scientific advice on the definitions of the terms used in the Federal policy statement?

Dr. RILEY. Not that I am aware of.

Mr. VOLKMER. And you do have some differences, listening to your testimony and reviewing your testimony, in regard to the subject matter to be reviewed?

Dr. RILEY. Yes, but I think it's fair to say that the differences that we have are relatively minor.

Mr. VOLKMER. Well, I agree, but there are differences.

Dr. RILEY. Yes.

Mr. VOLKMER. Yes.

And there is no question, Dr. Mellon, that you have serious reservations about USDA?

Dr. MELLON. I do.

Mr. VOLKMER. Well, Dr. Bentley will be up on our next panel, and we will discuss those with him.

Also, Dr. Riley, it's my understanding, in the process to be followed in the future—and Dr. Kingsbury, you correct me if I am wrong before Dr. Riley testifies, if I am wrong—that for research that's being done on genetic engineering where it's being funded by a Federal agency, that the Biosafety Committee of the facility where it's being done is basically the agency or the review process that's going to make the determination as to whether or not it's safe to go ahead and do this in a laboratory, et cetera. Is that correct?

Dr. RILEY. That's true for recombinant DNA work. That system was developed by the RAC as it matured in its process, so that a degree of decentralization came in and each campus where recombinant DNA work is being done has its own Institutional Biosafety Committee. I imagine that something similar can be developed in the case of organisms being introduced into the environment, but it doesn't exist at the moment.

Mr. VOLKMER. Dr. Kingsbury.

Dr. KINGSBURY. The introductions into the environment rise to the next level above the IBC. The Institutional Biosafety Committee would review that application but would not make a final determination. Introductions into the environment, under the current status with the NIH guidelines and all of the other policy, would go to a Federal review committee before that introduction would go on.

If you were doing an experiment that would ultimately go to the environment but you are not yet ready to go to a field test, those experiments could be reviewed by the IBC. But prior to any introduction to the environment, you would have to go to a Federal review committee.

I think this is a question that has come up in terms of agricultural research, but there are a large number of projects that have potential environmental introduction, assuming they're successful. Those have not been reviewed at a Federal level, but they have not been approved for environmental introduction. It's only at that stage that would go to the ultimate—to the Federal review.

Mr. VOLKMER. Who, Dr. Kingsbury, while the research is being done, is being funded, and it's being done within the laboratory, who reviews that to make sure that it's being done properly and that we don't have any problems with it or releases at that time?

Dr. KINGSBURY. Research—all forms of recombinant DNA research——

Mr. VOLKMER. Now, I am talking about Government-funded.

Dr. KINGSBURY. Yes.

Mr. VOLKMER. All right.

Dr. KINGSBURY [continuing]. Would be subject to IBC review until one reaches the level of an experiment that falls within the federally reviewed areas. That would be, in the case of some experiments with—if you were doing recombinant DNA experiments with a microbial toxin, if you were going to clone botulinum toxin, that is something that would come to Dr. Gartland and the Recombinant DNA Advisory Committee at NIH. If you had—if you were going to an environmental introduction of a microorganism or a plant, it would be reviewed at a Federal level.

If you were working on the derivation of a cloning vector to introduce a herbicide-resistant gene into a plant and the construction of that gene vector or the introduction into plant cells in culture would be experiments that had no environmental—direct environmental—introduction, those are experiments that would be registered with the Institutional Biosafety Committee and would fall under the institutional purview handed down to the institutions.

It's only when you were to go into classes of experiments that are considered hazardous—those that involve microbial toxins or other plant toxins as well, or into the environment—that you would go to a Federal level. This has been the longstanding practice of the RAC, and it's been very successful so far.

Mr. **VOLKMER**. All right, Dr.Riley, as one—as I understand, you serve as chairman of the Institutional Biosafety Committee at your university. Is that correct?

Dr. **RILEY**. That's true. Yes.

Mr. **VOLKMER**. In such capacity, you've had experience. Would it be possible for these committees, as they are presently structured, to take on the responsibility of certifying research proposals for compliance with the policy statement articulated by the various Federal agencies?

Dr. **RILEY**. I have wondered whether there might be a way for the IBC's to perform a constructive role at the campus level, but I am aware that there is—there have been no decisions along those lines yet. But I can see that there is in place a certain infrastructure that could be turned to constructive ends in this regard, just channeling reports, gathering—making sure that all the germane data has been gathered to forward to the Federal agencies. But I also can see that the individual IBC's cannot take any kind of definitive action in this arena at the present time.

Mr. **VOLKMER**. All right. Now, what, if you know of any, statutory restriction or gaps are there that inhibit USDA's Science and Education Division from reviewing proposals to license or release genetically engineered organisms? Does anyone want to answer that?

Dr. **MELLON**. Statutory restrictions?

Mr. **VOLKMER**. What restrictions or gaps? In other words, there are restrictions in the law, or nothing in the law that does anything, that would inhibit S&E from reviewing proposed license or release of genetically engineered organisms?

Dr. **MELLON**. I can't think of any specific restriction. I—the question is from where does it get its authority.

Mr. **VOLKMER**. I notice that in your testimony. Right.

Dr. **MELLON**. And it is simply providing an opportunity out of the goodness of its heart for companies to have their—their products reviewed. It doesn't have any authority for that review. It's not clear—it occurs to me, I was wondering what would happen if USDA were to face an AGS-type situation where the guidelines laid down, or the procedures established were violated.

I mean, what recourse would USDA have? EPA, acting under a very stringent and well-designed regulatory statute, could move and fine and use the power of the courts to make sure rules were adhered to. In the same situation, I don't think USDA would have any recourse other than persuasion.

Mr. **Volkmer**. OK.

Dr. **Mellon**. And perhaps just to shake its finger and say, "You shouldn't do that again." But it is not acting from any regulatory authority that I know of, in offering that review.

Mr. **Volkmer**. We have another vote on. I am going to have to recess. And since we possibly will have another vote after this vote—there's a strong possibility of that—since most of us haven't had lunch, you're not going to get a long time, neither will I, we will recess until 1:30. That gives everybody 45 minutes to try to get a little bit to eat and come back, and we will complete this panel.

Yes, I want this panel back. We're not finished.

[Whereupon, at 12:45 p.m., the subcommittees were recessed, to reconvene at 1:30 p.m., this same day.]

AFTERNOON SESSION

Mr. **Volkmer** [presiding]. The committee, the three committees jointly, will continue the hearing.

I would like to start with a comment that, Dr. Norse, you make in your statement. It says, "In my view, requiring rigorous review only for intraspecific transfers is still inadequate." That's commenting earlier on what you proposed instead of just intrageneric. "Certain advocates of genetic engineering have two banners that they wave vigorously at meetings whenever the opportunity arises. One is, 'Regulate the product, not the process.' " And as a person who has heard that several times at these hearings, I agree with you.

But, you say, "Without commenting on the wisdom of this slogan, I would point out that the BSCC framework and exempting deletions of genes and transfers of genetic regulatory sequences is emphasizing process over product."

Dr. Riley, do you agree with that?

Dr. **Riley**. No, I don't think process is involved in that particular distinction. I think there are two kinds of genetically-altered organisms that Dr. Norse is talking about there: one where there is a deletion and the loss of a gene. That can come about either by the new technology or by old methods of mutation. Then the other is putting a foreign regulatory gene in front of another gene. So those are two different—the deletion and the regulatory sequences are two different kinds of microorganisms, that both can be made either by the old technology or the new technology.

Mr. **Volkmer**. Yes, but the question is, Is that a process or is it a product?

Dr. **Riley**. The organism that has a moved regulatory gene is a product. The organism that has a deleted gene is a product. The process is whether it was made by old technology or new technology, biotechnology. But you can get to the same end point in two different ways: either using the new, which is more accurate, or the old, which is more or less at random and then pick out the product that you want. But a deleted organism is a product, and an organism with a moved regulatory gene is a product.

Mr. **Volkmer**. All right.

Dr. Kingsbury, I guess you would agree with Dr. Riley?

Dr. **Kingsbury**. Yes, sir. [Laughter.]

She stated it very, very well.

Mr. **Volkmer**. Do you have any further comment, Dr. Norse?

Dr. **Norse**. I think the emphasis here seems to have been on the processes by which we could get to these end points. The emphasis hasn't been exclusively on the end points. Transferring genes from one organism to another within a genus may or may not occur in nature, it may or may not be able to be achieved by conventional means of genetic manipulation, it may require the new techniques that have been developed within the last 10 to 15 years. But it seems that the tone of the regulation emphasizes more the process. If you are going to delete something, if you're going to transfer a regulatory sequence, then it is not subjected to the higher level of review—not emphasizing the product.

I think things get a bit muddied there, and I am—I don't know that I can comment on the wisdom of one versus the other, but it doesn't seem to be consistent. The specific proposals don't seem to be consistent with that approach that I have heard articulated so many times in the last 2 years.

Mr. **Volkmer**. Dr. Mellon, do you wish to comment at all? You don't have to.

Dr. **Mellon**. Only to say that the agencies have obviously adopted both approaches. I mean, the definitions embody both approaches: the definition of a new organism as one that contains genetic material from dissimilar parents is a definition based on process; and the definition of an organism as a pathogen is one that—that is one based on the property of the product regardless of how it was made. So the definitions used in this framework embody both approaches.

Mr. **Volkmer**. So we are not necessarily into the definitions staying with the slogan, "Regulate the product, not the process"?

Dr. **Mellon**. Right. Right.

Mr. **Volkmer**. Dr. Kingsbury?

Dr. **Kingsbury**. I think that that is an accurate characterization. If I can just step back from this for a minute. You know, why are we really here talking about biotechnology products? I mean, what is it that characterizes this particular debate and what has characterized the debate all along?

The characterization is concern about novel—novel combinations of genes, things that would not occur under natural conditions, things that we fear may need oversight because we're putting together unusual characteristics. That's really the core of this question, I think: that traditionally as long as humans have learned how to harness microorganisms and other organisms, we have been able to use them to our benefit in the environment. That's an old issue; that's really not the new one.

The new one is the uniqueness of the organisms. One has to keep in mind in the regulatory framework that that is, in fact, the central question. So the notion of an intrageneric combination addresses that question. From that point of view, this must be a process-oriented regulation. Those are the unique things; those were what we were concerned about.

When one has products that may arise by natural processes, then the regulation should be the regulation that is product-oriented, that we have been using traditionally. For example—which is a difficult example, but I will throw it out; I don't think that any of us wants to go into the details of all of this. But let's assume that we have the pseudorabies vaccine, a deletion mutant, a deletion mutant that could occur naturally, but it can occur much more directed and much easier, using this new technology; not a unique product that was produced, because we've discovered restriction enzymes. It could have been produced, and in fact many of these had been produced by the old technologies. That regulation is by the product. That is an animal pathogen. It's going to become an animal biologic. It needs to be safe, and it needs to be effective—standard regulatory approach.

There is nothing unique about the biotechnology background for that particular product, and I think that's what we were trying to address here. One sees the combination as has just been characterized of product regulation for those products that could occur under natural conditions, and process-type regulation for those things that are unique or potentially unique because of the technology that's arrived from recombinant DNA. I think that's the reason why you see this mixture.

Mr. VOLKMER. All right. Then, Dr. Kingsbury, along that line, why has the BSCC in the guidelines excluded from full review intergeneric organisms created by adding so-called non-coding regulatory sequences when these sequences can drastically alter an organism's production of various proteins?

Dr. KINGSBURY. As I mentioned earlier, that approach to dealing with recombinant organisms was one that was developed during the recombinant DNA guidelines developed by the NIH/RAC over a period of time. It was based on their feeling and the observations of the scientific community during the debates that went on at the time of the guidelines' development, that these did not constitute an unusual mixture of characteristics, but simply changed in a way that could occur naturally, in fact, the regulation of a given product, a given gene product.

Again, one finds in nature unusual mutations for regulatory sequences. That's how we discovered regulatory sequences, in fact, because of mutations that occurred in those sequences and changed regulation. That was not an unusual sort of approach.

Mr. VOLKMER. Any other panel member wish to comment on that? Dr. Riley?

Dr. RILEY. I think that the ASM would like to establish again its position on this, which is that we recognize that rather quickly, probably, recombinants involving regulatory sequences, after being studied and examined, would probably find themselves on a list of safe recombinants.

Nevertheless, I think we will stick with the position that we believe that recombinants formed with coding and noncoding sequences foreign to the organism should be examined at the same level of seriousness at the outset until an exempt list is made up.

Mr. VOLKMER. In other words, you would be going on a case-by-case review until we had more of a history——

Dr. RILEY. That's right.

Mr. Volkmer [continuing]. Basically on it?

Dr. Riley. And to treat them as seriously as any other gene at the outset, anticipating exclusion later.

Mr. Volkmer. In other words, you put a little caution in this?

Dr. Riley. That's right.

Mr. Volkmer. Dr. Mellon.

Dr. Mellon. I agree.

Mr. Volkmer. Now, as I understand it, Dr. Kingsbury—and I am going to ask Dr. Moore about this when he gets here—EPA's policy statement allows producers to provide for publication in the Federal Register of generic descriptions of microorganisms whose identity and/or use is claimed to be confidential business information.

How can a generic description omitting identity and use give the public adequate notice of the nature of the organism being reviewed so they can comment on it? I am not a scientist, so I would like to know.

Dr. Kingsbury. I have not—I don't know the details of what their plan is for this publication in terms of what information would be provided. So that is a difficult question to answer.

It seems to me that one could provide a great deal of information without giving the exact strain of the microorganism, which I think is what the "confidential information" would like to keep confidential and still provide a good deal of information about what the characteristics of the organism would be: in the case of a pesticide, what the pesticidal activity is; in case of the organism, what its life history had been prior to the genetic modification. Those are basically the pieces of information, I think, that people would like to have.

Mr. Volkmer. Dr. Mellon or Dr. Riley, would you like to comment on that?

Dr. Mellon. I simply want to acknowledge that the confidential—the confidentiality of data is an extremely important and very difficult issue. I think companies have a legitimate proprietary interest in the information that they've developed as part of a product development.

At the same time, the public has a legitimate interest in the safety of the products that the companies are developing, and in the case of biotechnology it's extremely important that the public has an opportunity to see what these—to see what the products are and to judge what risks they present.

I have always been concerned that 5 years are going to elapse and that 20 organisms are going to have been reviewed and released into the environment that nobody is going to know what they are, where they've been released, and what's happened after they've been released, because all that information is going to be withheld by an agency as confidential information.

If at the end, if that scenario is a correct one and the 5 years do elapse and an agency stands up and tells the public that the technology is safe, "Don't worry about a thing," I don't think that they're going to be believed. I think it's in the industry's interest as well as in the public's interest to try to resolve this; this conflict of interest here and arrange procedures by which members of the public can have access to the health and safety information that the companies develop.

Mr. **Volkmer**. Dr. Riley.

Dr. **Riley**. I have nothing to add to that.

Mr. **Volkmer**. All right.

Now, under TSCA, EPA has defined intergeneric organisms as "new" substances subject to premanufacturing notification requirements, and all other organisms as "existing" organisms not subject to such requirements. Is this distinction workable and scientifically valid? Dr. Riley?

Dr. **Riley**. In the main, I think, yes, although it grates a little on the nerves of some scientists to characterize a living organism as a new substance in the same category as new toxic chemicals. So it bothers us a little in the sense that that's not the way you would define it if you were starting from scratch.

Nevertheless, it does seem to be a relatively workable way of going about it: that is, the newest thing you can do in genetics is to put two genes together that would never come together otherwise, and so you can see that then, one can view it as a new chemical. "Chemical" is just a terrible word. It's a new organism. [Laughter] But in view of the fact that these people are working with an existing statute and with TSCA, I think that they've done the best that could be done.

Mr. **Volkmer**. But we still have only a notification system rather than a permit system. Does that give you any concern?

Dr. **Riley**. No, it doesn't give me concern, because if a dangerous organism were to be submitted in a premanufacturing notice to the RAC-like committee that would be formed to look at it, then I take it on faith that if there were danger involved, that RAC-like committee would impose certain requirements before that organism could be deployed to the environment.

So I can see that a PMN can actually function in a set of regulatory—I started to say "regulatory regulations;" that doesn't leave me with a very good sentence—with regulations. I can see that it could be made to work, yes.

Mr. **Volkmer**. If sufficient information is provided in the prenotification?

Dr. **Riley**. Yes.

Mr. **Volkmer**. There would have to be that?

Dr. **Riley**. And that would have to be stipulated, yes, by the agency, what information is needed.

Mr. **Volkmer**. Dr. Mellon.

Dr. **Mellon**. It does give me some pause. I am generally convinced that EPA is going to use the authority that it has under TSCA to vigorously regulate the products that come under its jurisdiction.

But it troubles me that if EPA should fall down on the job, an organism could be developed, notice given to EPA, no review conducted, and if EPA doesn't step in and do something about it, that organism will go on the inventory totally unreviewed and no one will have—that will be perfectly legal. No one will have any recourse; no one will be able to complain. You will be able to complain to EPA that it didn't do what you think it should have done, but you will not be able to go to court and charge it with failure to carry out a statutorily imposed duty.

Mr. **Volkmer**. Now, as I understand it, Dr. Kingsbury, Dr. Bentley is the head of the subcommittee or committee that's exploring the definitions of "release" and "containment"? Is that correct?

Dr. **Kingsbury**. Dr. Bentley is co-chair with Dr. Moore.

Mr. **Volkmer**. Fine. We will have them both up. Because I just renoticed something that is in Dr. Riley's statement. That, you know, to me it seems that there should be a lot of study at least on this much—and maybe there is. "According to our view, spraying a suspension of microorganisms on field plants or inoculation of plants or animals that then have access to the outdoors constitutes release."

Dr. **Riley**. Yes.

Mr. **Volkmer**. Do you agree on that? You made—that statement, do we agree on that or disagree?

Dr. **Kingsbury**. [Inaudible.]

Mr. **Volkmer**. Pardon?

Dr. **Kingsbury**. I believe that with the proviso that I think, as Dr. Riley had pointed out in her last appearance before the committee, that there are instances where one could envision an engineered vaccine that doesn't——

Mr. **Volkmer**. No shedding?

Dr. **Kingsbury**. Right. There is no shedding. I think that was one case where you would say that does not constitute an environmental release. If it's a genetically engineered Sabin-type vaccine, where in fact the release is an integral part of the effectiveness of the vaccine, then you're absolutely right.

Mr. **Volkmer**. And a "containment facility is a laboratory, greenhouse, or other chamber in which microorganisms are confined and can be monitored under controlled conditions." Anybody disagree with that statement?

Dr. **Mellon**. No. But more work needs to be done on that definition.

Mr. **Volkmer**. Well, I am just saying that those two statements in itself to me seem to be kind of a starting point, surely.

Well, what concerned me, Dr. Kingsbury, is, in reviewing your earlier—your testimony—is that it's going to be a year from now before we get these finalized. That's correct?

Dr. **Kingsbury**. That's correct. That was the estimate that we made.

Mr. **Volkmer**. I know we have to go through a regulatory process and that takes time and everything. But that does concern me that, again, as a nonscientist looking at it, and who has looked at this thing now for some time, that I don't know where all the problem is to arrive at those two definitions. I just don't see why it would take a year.

Dr. **Kingsbury**. It's a process delay rather than a substance delay. I mean, right now in the Environmental Protection Agency statement we have a coverage of contained—they have defined "contained," and it's a workable, clear definition. It's a quite conservative one.

We have now gone back to review this problem again to see that it is the correct one and to try to work with the agencies to set some specific technical standards, is what we're really talking about here. We want broad public participation, and that is—that is a slow process. It's a question of how open the process is, and we're trying to balance those two—those two problems off against each other: speed versus openness. Democracy moves slowly sometimes.

Mr. **Volkmer**. In other words, we have caution on that side, and I can respect some of that caution. But I think we should go along, maybe you should review some of the things that have been said here by the others as to caution on the other side also, some of the definitions and such.

Now, under the policy statement, genetically engineered organisms used in closed manufacturing systems in industry may be exempt from scientific review prior to use. Correct?

Dr. **Kingsbury**. Yes.

Mr. **Volkmer**. The Occupational Safety and Health Administration has been under increasing criticism in recent years for its inability to fully inspect industrial plants and protect workers from chemical hazards in the workplace. As a member of Congress who has been working on that area and certain areas—I know we have legislation probably coming up in the not-too-distant future on the floor to try to correct some of that—what concerns did the BSCC have regarding OSHA's ability to inspect the workplace to protect workers from biohazards?

Dr. **Kingsbury**. This was an issue that was discussed within the context of the existing manufacturing situation. As you know, the FDA has had a long history of fermentation technology that it has had oversight of. There has been a long history of fermentation technology in a variety of areas. There are in place a variety of fermentation processes involving highly pathogenic organisms that are commonplace today, and to the best of our knowledge, we really have not seen a problem that has resulted from that current technology.

It appears that the existing containment technology available to manufacturers and the ability of OSHA to monitor that, together with the Food and Drug Administration in terms of pharmaceuticals, has not failed us in any way that I am aware of. And the result of our discussion was that people felt comfortable with OSHA's ability to deal with that issue right now and that a change in that was not necessary.

Mr. **Volkmer**. In other words, what I am hearing—correct me if I am wrong—is that we really don't have that much problem in the workplace and OSHA can take care of what little problem there is?

Dr. **Kingsbury**. That was our—that was our perception of this particular area. You know, we're talking about confining our examination to microbes in the workplace, and at least to my knowledge, there has not been a problem with this, even though many of the microbes that are now used in large-scale processes are pathogens.

Mr. **Volkmer**. Now, Dr. Kingsbury, I am sure you have read the article—and I had a copy of it here—a recent issue of the National Journal on biotechnology development. You are quoted as saying that, "If we approach biotechnology as dangerous, we will never get anywhere." Is that an accurate quote? I always ask that before I ask the question—as one who has been misquoted more than once. [Laughter.]

In all fairness.

Dr. **Kingsbury**. I will pass on that one. Go on to the question. I have been known to say all kinds of things.

Mr. **Volkmer**. Well, how would you characterize the philosophy underlying the policy statement developed by the BSCC?

Dr. **Kingsbury**. I think that I would really—I think I made the comment earlier, I believe that this has been a caution—a cautionary approach, that we have not decided, as we could well have and as some of our—as Dr. Norse commented, or those in the molecular biology community who really believe, that no hazards are introduced by this kind of technology.

Let's remember that since 1972, when this—when recombinant DNA technology was becoming more widespread in use and in that period of time, we have now seen a technology that was an oddity, that was only done in a couple of laboratories in Stanford and San Francisco, wide debate about its safety, move into a situation where it is now one of the core technologies used in all areas of biomedical research. It has spread throughout the academic community so that I don't know of a research university department of biology, biochemistry, molecular biology, or bacteriology that doesn't have at least some of its investigators using this recombinant DNA technology as a tool. It is very widespread. We have yet to see a real problem.

I think that my concern is that we declare it dangerous when in fact we have no direct evidence that it is a dangerous technology. That's not to say that we should not approach environmental release of these microorganisms which are unique in their structure, with caution. I fully support that. I know that the entire working group came to this process with that notion. We don't have any question about it.

But at the same time, to a *priori* make the declaration that it's a dangerous technology I think is overstating it. There is simply no evidence that in fact it is dangerous.

Mr. **Volkmer**. Well, I won't disagree with you that all products of biotechnology aren't dangerous, but I think there are products that can be dangerous. And I think it would be wrong to take the philosophy in developing the guidelines that they are all safe until somebody proves that they're not safe, as well as—

Dr. **Kingsbury**. That's right.

Mr. **Volkmer** [continuing]. The philosophy that they're all dangerous until somebody proves that they're not dangerous, I think.

Dr. **Kingsbury**. Well, I think the guidelines work from the—do not come from the position that they're all safe until proven dangerous. I think that these are stringent guidelines. Every microorganism would be reviewed before it could go into the environment. That is a philosophical statement that, in fact, caution is absolutely necessary, and I think that's the position that we have all taken.

Mr. **Volkmer**. Well, I think, Dr. Kingsbury, I think perhaps there has been a little disagreement among this panel as to some of those things and the necessity or maybe perhaps how extensive review there should be of some of them. So we will be reviewing that ourselves and determining in the future whether we should take any action or not.

With that, I want to thank the panel sincerely. I am sorry you have been here so long, but you have been very good and have been very helpful to us.

We will proceed with our third panel. We have Dr. Jack Moore, Environmental Protection Agency; and Dr. Orville Bentley, from the U.S. Department of Agriculture. As I understand, Dr. Bentley will be accompanied by Dr. Jordan and Dr. Mikshe. And Karen Darling.

Dr. Moore, you may proceed with your statement. All the statements which will be submitted will be made part of the record at this point in the record, at the point of your testimony, and you may either review or summarize the statement or review it in full, however you so desire.

Dr. Moore.

STATEMENT OF DR. JOHN A. MOORE, ASSISTANT ADMINISTRATOR FOR PESTICIDES AND TOXIC SUBSTANCES, U.S. ENVIRONMENTAL PROTECTION AGENCY

Dr. MOORE.[1] Mr. Chairman, I would like to just highlight a couple of points that are in my testimony.

As the committee well knows, in December 1984, EPA proposed an approach to the regulation of biotechnology products under two statutes that it administers; the Toxic Substances Control Act as well as the Federal Insecticide, Fungicide, and Rodenticide Act.

EPA received comments from 71 organizations and individuals addressing a broad range of scientific policy issues after promulgation of that statement.

The elements—I am sorry—the comments proved to be extremely valuable to EPA in developing its current policy and, in fact, led EPA to revise its original proposal in certain significant respects. EPA's current policy, as described in the June 26, 1986, Federal Register notice, is based on public comments, discussions with many scientists, and experience in reviewing genetically altered microbial products during the year or year and 3 months that intervened between the two notices.

Probably the most significant change is that EPA has established different levels of review for different types of microbial products. In its 1984 proposal, it proposed to subject all genetically engineered microorganisms to the same level of regulatory scrutiny.

Based on comments that had been received, and further reflection on that point, we have tried to develop and have promulgated a system that basically tries to tailor the level of review to the nature of the change that was effected using biotechnology, and the degree of risk that may possibly be associated with the use of that material.

The agency's conclusion is that there are primarily three categories of microorganisms that currently deserve the closest regulatory attention. These three types that we will most closely review under both FIFRA and TSCA are: microorganisms with new characteristics or that are new to the environment in which it is proposed to be used; microorganisms that have hazardous components in them, either they are pathogenic or received something from a pathogenic organism; or, third, microorganisms that are used in the environment—and parenthetically, they therefore have the potential for widespread exposure.

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[1] See appendix 5, p. 184; for edited oral remarks of Dr. Moore.

Now, to translate that general approach into the Toxic Substances Control Act, we basically are talking about microorganisms that would be altered through deliberate human intervention to contain genetic material from dissimilar source organisms. They would be considered new, which is a critical component for being captured under TSCA. Therefore, it would be subject to premanufacture notification requirements.

EPA, and the other regulatory agencies as well, define the word "dissimilar" as organisms from different taxonomic genera. The organisms resulting from such a combination then would be called "intergeneric."

Now, in order to implement this, we basically are going to have to get into four rule promulgations. Very briefly—which are also described in my written statement—we are going to have to get into a rule that allows PMN review during the early stages by making a modification to the current research and development exemption.

Second, we're going to write a significant-new-use rule that will basically allow us to confront and review altered genetic material that have come from the pathogenic organism sources.

Third, at the lower level of review, we're going to promulgate a rule under section 8(a), which basically is a requirement that people will notify EPA in advance of any proposed field experiments.

Then, lastly, we are also entertaining the possibility that we might exempt certain types of organisms under section 5(h)(4) of the Toxic Substances Control Act. Whether we do that and how we do that will be strongly contingent on the nature of the comments that we have asked to receive in our June 26 notice. Since we haven't received those comments yet, we certainly can't draw judgments as to how, if, and under what set of circumstances we would do such.

EPA's current policy under FIFRA modifies the scope of what was the interim policy by providing again for these two levels of notification and review. The three categories of microorganisms that would deserve the closest degree of scrutiny are similar to that which I have just described that would be appropriate to both TSCA and FIFRA.

We shouldn't lose sight of the fact that it has always been the case that FIFRA's experimental use permit provisions must be observed for all pesticides, regardless of whether or how they were manipulated, prior to field tests involving anything greater than 1 acre of water or 10 acres of land.

Again, the level and type of review that we will give are the same under EPA's current policy as well as it was under the interim policy. In essence, we have solicited and have been successful, I believe, in getting scientists who possess expertise appropriate to the specific issue to partake of their time to give us the benefit of their expert opinion as well as the opinion of agency scientists during the evaluation of these pesticides. This has been done on an ad hoc basis under the aegis of the Scientific Advisory Panel which is mandated under FIFRA. I think that process has worked well. We intend to continue to use that process in the throes of promulgating a Biotechnology Sciences Advisory Board on behalf of the whole agency—so that function probably will transfer from the Scientific Advisory Panel on an ad hoc basis under this new committee that is in the process of being formed.

EPA feels that its policy ensures that those biotechnology products that currently deserve close scrutiny will be properly reviewed. I might parenthetically say that they are being properly reviewed, given that we have looked at nine submissions in the last year under the pesticide program, and that future changes to the regulatory program can be adopted, and that clear guidance is available to this young, but important and vulnerable industry.

The agency believes that its policy will help the public to understand that the products of genetic engineering encompass many possibilities, many of which are of modest or minimal concern. Therefore, the products' characteristics should determine the appropriate level of scrutiny in this case by the Federal Government.

That concludes my statement, Mr. Chairman.

[The prepared statement of Dr. Moore follows:]

TESTIMONY of JOHN A. MOORE
ASSISTANT ADMINISTRATOR FOR PESTICIDES AND TOXIC SUBSTANCES
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
SUBCOMMITTEE ON INVESTIGATIONS AND OVERSIGHT,
THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT,
AND THE
SUBCOMMITTEE ON SCIENCE, RESEARCH AND TECHNOLOGY
OF THE U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE AND TECHNOLOGY

July 23, 1986

Good morning. My comments this morning will focus on the Environmental Protection Agency's (EPA) policies that apply to biotechnology. As you requested, I will give particular attention to those aspects of our current policy that have been significantly modified since publication of our "Proposed Statement of Policy on Biotechnology" in December, 1984.

In December of 1984, EPA proposed an approach to the regulation of biotechnology products under the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). These are the two statutes that EPA administers that provide it with authority over certain biotechnology products prior to their release in the environment or their commercial use and manufacture. EPA received comments from 71 organizations and individuals addressing a broad range of scientific and policy issues. Among other things, commenters addressed the issues of EPA's authority to regulate biotechnology products, the scope of EPA's proposed policy, the proposed product-by-product review procedures, and the possible economic impact of EPA's policy on the new biotechnology industry. The comments proved to be extremely helpful to EPA in developing its current policy and, in fact, led EPA to revise its original proposal in certain significant respects.

EPA's current policy on biotechnology, as described in the June 26, 1986 Federal Register, is based on public comments, discussions with many scientists, and experience in reviewing genetically altered microbial products over the last year. It reflects some important steps forward in the evolution of the public debate over risks of genetically engineered organisms. The most significant change is that EPA has established different levels of review for different types of microbial products. In its 1984 Proposed Statement of Policy, EPA stated its intention to subject all genetically engineered microorganisms to the same level of regulatory scrutiny. Many of the public comments that EPA received were critical of this approach. Commenters stated that many genetically engineered microorganisms are similar or identical to microorganisms that occur naturally, and that only a subset of genetically engineered microorganisms actually have new combinations of traits. In addition, commenters felt that whether a microorganism has been genetically engineered or not is an insufficient indicator of its potential to cause harm. They urged the Agency to identify categories of genetically engineered microorganisms that present higher and lower risks, and to establish regulatory programs accordingly.

In response to these concerns, EPA conducted a thorough review of its options for implementing FIFRA and TSCA in the biotechnology area. The Agency's conclusion is that there are three categories of microorganisms that currently deserve the closest regulatory attention, but that it is also necessary for the Agency to monitor environmental uses of microorganisms in general. The three types of organisms that EPA will most closely review under both its FIFRA and TSCA statutes are microorganisms with new characteristics or that are new to the environment in which they will be used (and whose behavior is therefore less easily predictable), microorganisms that have hazardous components (pathogens or organisms containing genetic material from pathogens), and microorganisms that are used in the environment (and therefore have the potential for widespread exposure).

The three areas of higher concern that EPA has identified are based on the current level of knowledge in this rapidly developing area. EPA recognizes that there is still uncertainty, and has therefore taken several steps to address that uncertainty. First, EPA is using various statutory mechanisms to ensure that it receives reports from all persons directly releasing microorganisms to the environment, whether the microorganisms are engineered or not, in advance of any such release. The only exception is that indigenous, nonpathogenic microorganisms may be released for small scale field testing purposes under FIFRA, but even these must be reported as soon as larger scale uses are intended. The Agency will have a short period of time to review the report and to take steps to prevent the scheduled release if there appears to be any risk involved. In addition, these procedures will decrease the uncertainty about risks because they will increase the Agency's data base on the types of microorganisms being used, their characteristics, and their potential for causing adverse effects. Second, EPA has explicitly acknowledged that biotechnology (and particularly genetic engineering) is an emerging and rapidly developing technology, and the Agency has designed its policy so that it can evolve along with the state of scientific knowledge.

EPA is relying on a number of its authorities under FIFRA and TSCA to implement its overall biotechnology policy. The next part of my testimony addresses the authorities and approaches more fully for each of the two statutes.

Under TSCA, microorganisms altered through deliberate human intervention to contain genetic material from dissimilar source organisms are considered "new" and subject to premanufacture notification (PMN) requirements, if they are manufactured for TSCA purposes. EPA (and the other regulatory agencies) define "dissimilar" as organisms from different taxonomic genera; the organisms resulting from such a combination are called "intergeneric." EPA will supplement this PMN policy in four ways. First, it will require that a PMN review be conducted prior to the environmental release of any "new" microorganism. This will be accomplished by amending the PMN rule to eliminate the current exemption for research and development. Second, the Agency will issue a Significant New Use Rule covering microorganisms that are pathogens or have been deliberately altered to contain genetic material from pathogens. Microorganisms covered by the Significant New Use Rule will also be reviewed before environmental release. Third, all other microorganisms deliberately released to the environment will be subject to a lower level of reporting requirement under TSCA section 8(a). Finally, section 8(e) of TSCA, which requires reporting of significant risks, applies to all microorganisms subject to TSCA.

To reduce the regulatory burden as much as possible, EPA is taking additional specific steps. First, certain exceptions to the above catogories of general concern have been described in the Agency's policy and are therein excluded from the areas of higher consideration. In addition, EPA intends to use its authority under section 5(h)(4) of TSCA to exempt certain inter-generic (new) organisms from PMN reporting. For example, EPA is considering an exemption for contained uses of inter-generic microorganisms that have a long history of safe industrial use.

Next I will turn to FIFRA, which applies to microorganisms used as pesticides. In October, 1984, EPA announced that under FIFRA, persons intending to conduct small scale field tests of genetically altered and nonindigenous microbial pesticides must notify the Agency at least 90 days in advance, to allow the Agency to determine if an Experimental Use Permit (EUP) is necessary. Since that time, EPA has received nine notifications from companies and individuals seeking to conduct small scale field tests with such microorganisms. Three EUP applications have actually been submitted and reviewed. These reviews and most of the materials pertaining to these submissions are publically available.

EPA's current policy under FIFRA modifies the scope of the interim policy by providing for two levels of notification and review. The three categories of microorganisms deserving closest regulatory attention, that I previously described, will be subject to the original procedures under the interim policy: 90-day notification and review to determine if an EUP is required. However, there will now be an expedited, 30-day review for all other genetically engineered or nonindigenous microorganisms. At the end of the 30-day review, EPA will determine whether or not a full notification is required, or whether the experiment may proceed without further review.

As has always been the case, FIFRA's Experimental Use Permit provisions must be observed for all pesticides, regardless of whether or how manipulated, prior to field tests involving greater than ten acres of land or one acre of water. This generally means that the applicant must submit information to the Agency in accordance with the regulations on data requirements under FIFRA (40 CFR Part 158). Similarly, all pesticides must be registered by the Agency before they can be sold or distributed.

The level and type of review that EPA accorded to the microbial pesticides submitted by Advanced Genetic Sciences, Dr. Lindow, and Monsanto Corporation are the same under EPA's current policy as they were under the interim policy. Recognized scientists possessing expertise pertinent in the review of each submission were consulted during evaluation of these microbial pesticides on an ad hoc basis. Included were members of the EPA Scientific Advisory Panel, a statutory advisory group to the EPA Administrator. EPA will continue to seek the best scientific expertise available in its reviews of biotechnology products. As part of EPA's efforts to obtain the best scientific advice available, EPA is in the process of instituting a Biotechnology Science Advisory Committee. This committee, which will be composed of nine scientists and two representatives of the public, will analyze problems, conduct reviews, and offer recommendations.

EPA believes that its policy brings a sharper focus to the underlying issues of concern about genetic engineering. The policy ensures that microorganisms that are likely to raise questions about their effects on humans or the environment will receive close scrutiny; it also ensures that lower risk applications are appropriately monitored. The policy will not discriminate against engineered microorganisms simply because of the methods used to manipulate them. For example, the policy acknowledges that microorganisms that are capable of causing disease or that are used in environments where they did not previously exist, are also of sufficient concern that they deserve to be carefully reviewed, even though they may not be engineered. It also addresses the fact that many engineered organisms are virtually identical to organisms that occur in nature, and that they therefore deserve essentially the same level of regulatory attention as their natural counterparts. Thus, organisms that are genetically engineered but otherwise have no apparent risk factors, will receive an expedited level of Agency review.

In addition to developing its internal procedures, EPA has reached agreement with the Department of Agriculture to eliminate duplicative requirements wherever possible, and to coordinate reviews where overlaps could not be avoided.

EPA's policy ensures that those biotechnology products that currently deserve close regulatory scrutiny will be properly reviewed, that future changes to the regulatory program can be adopted, and that clear guidance is available to this young, important, and vulnerable industry. The Agency believes that its policy will help the public to understand that the products of genetic engineering encompass numerous possibilities, many of which are of modest or minimal concern, and that the products' characteristics should determine the appropriate level of Federal scrutiny.

This concludes my formal statement. I will be pleased to answer any questions from members of the Subcommittees.

Mr. **Volkmer**. Thank you very much, Dr. Moore.
Dr. Bentley.

STATEMENT OF DR. ORVILLE G. BENTLEY, ASSISTANT SECRETARY FOR SCIENCE AND EDUCATION, U.S. DEPARTMENT OF AGRICULTURE, ACCOMPANIED BY KAREN DARLING, DEPUTY ASSISTANT SECRETARY FOR MARKETING AND INSPECTION SERVICE

Dr. **Bentley**. Thank you, Mr. Chairman. I will cover some aspects of questions that were raised in the letter and some brief remarks. Karen Darling will answer not only questions dealing with the Department but more oriented toward the regulatory side and mine toward the research side. So my comments will be an attempt to respond directly to the questions that were posed.

The first question in the letter asked about whether or not the guidelines will provide the USDA with clear and sufficient authority to review deliberate-release proposals. It is the opinion within the USDA that we do have—that the guidelines do provide for this and for the necessary arrangements to handle our responsibilities and the authority clear and sufficient to handle these tasks.

We also comment that the coordinated framework for regulation of biotechnology will serve not only to coordinate activities among agencies, but it is certainly very helpful to us in USDA as we develop procedures for the handling of biotechnology research and product requests.

You also asked us to discuss the role of the research and regulatory divisions of the USDA and whether or not they have been coordinated. First, we are developing good working procedures within the Department for handling of applications. On the 14th of July, Secretary Lyng issued a Secretary's memorandum 1020-27 that formally established the Office of Agricultural Biotechnology. We have—I have included a copy of this document with the testimony.

This action centralizes the responsibility for implementing and coordinating the department's policies and procedures pertaining to all facets of agricultural biotechnology in one office.

We are in the process of initiating plans to obtain a full-time director for the OAB, but in the meantime I am functioning as the interim director, and through the assistance of the Food Safety and Inspection Service, Dr. Dan Jones is serving as an interim deputy director.

The department has also established some requirements whereby notices of all applications or requests received by USDA for licenses, permits, or approvals of agricultural biotechnology products or research that fall under the coverage of the June 26 Federal Register notice are to be forwarded to the OAB.

Also, no license, permit, or approval shall be granted by the USDA for any agricultural biotechnology product or research without review of the director for compliance with departmental policies and procedures. And we have attached a copy of this statement to our testimony.

Also, the department is in the process of establishing the Committee on Biotechnology in Agriculture that is called for in the guidelines. This committee will take the responsibility of establishing—or enhancing, rather, the coordination between the research and regulatory agencies and provide—serve as an advisory body within the department.

The CBA will be cochaired by the Assistant Secretary for Marketing and Inspection Services and by the Assistant Secretary for Science and Education. The membership of the committee will be policy-level representatives of the cogent agencies; namely, ARS, the Cooperative State Research Service, the Animal and Plant Health and Inspection Service—APHIS—and the Food Safety Inspection Service, and the U.S. Forest Service. We think this will be very helpful to us.

When fully implemented, the OAB will perform a staff role for the CBA. Whenever OAB believes that the proposed agency actions affecting biotechnology require decisionmaking at the assistant secretary level, it will refer such matters on a case-by-case basis to the CBA for resolution by the two assistant secretaries.

The next portion of my statement is a summary, as requested, of general points relative to the Federal Register notice of December 31, 1984. I will just touch on a few of those.

We think that the new document provides new information in both areas for regulatory and research responsibilities in biotechnology. It includes a discussion of the assignment of responsibilities within USDA for the oversight of USDA research and regulation of products of biotechnology. We think this is helpful—it has been very helpful to us as we work out the assignment of responsibilities and it should be very helpful to the private sector as they seek advice and review and approval of biotechnology applications.

Another section of the USDA policy describes the USDA's action regarding agricultural biotechnology research. The USDA publishes a companion document in the same Federal Register notice—USDA guidelines for biotechnology research that will closely parallel the NIH guidelines. The USDA guidelines will be issued under the authority of the Food Security Act. This act was amended—or in this act, section 1404 of the National Agricultural Research and Extension and Teaching Policy Act. The amendment gave the Secretary of Agriculture responsibility for establishing "appropriate controls with respect to development and the use of the application of biotechnology to agriculture."

Just as a further note and the comment that I have made on prior occasions before this committee, Mr. Chairman, that all USDA-funded agricultural biotechnology research or research conducted at an entity receiving USDA funds will be subject to the USDA guidelines for biotechnology research unless the specific research project is supported by and subject to the guidelines or regulation of another Federal agency.

The USDA hopes that entities not required to comply with the guidelines will voluntarily adhere to the requirements. To encourage compliance, the USDA proposes to adopt the NIH policy of providing researchers not required to comply with these guidelines the opportunity to have their new biotechnology research proposals reviewed by the USDA.

Just as in the NIH/RAC, a peer review process will be an important part of our activities. We are in the process now of establishing the Agricultural Biotechnology Recombinant DNA Advisory

Committee, ABRAC, which will have responsibilities for agriculture similar to and in many cases formerly handled by the NIH/AC over the past several years.

I think these points hit on—respond to some of the specific questions. At least that was our intention. We are pleased to answer any questions.

[The prepared statement of Dr. Bentley follows:]

United States Department of Agriculture

Statement of Orville G. Bentley

Assistant Secretary for Science and Education

Before the House Committee on Science and Technology, July 23, 1986

Subcommittee on Investigations and Oversight

and

Subcommittee on Science, Research and Technology

and

ubcommittee on Natural Resources, Agricultural Research and Environment

Mr. Chairman and Members of the Committee, we appreciate the opportunity to appear before you today to discuss the Coordinated Framework for the Regulation of Biotechnology as published in the Federal Register on June 26, 1986.

This document is the result of many months of work by several agencies, including the U.S. Department of Agriculture (USDA). These agencies have recognized the need to ensure a consistent Federal government approach to the development, regulation and safety of biotechnology research and products.

I want to begin my formal statement by first answering your question as to whether the guidelines will provide USDA with clear and sufficient authority to review deliberate release proposals. In the opinion of those within USDA who are charged with the responsibility of reviewing such proposals, the authorities are clear and sufficient to the task.

The Coordinated Framework for the Regulation of Biotechnology will serve not only to coordinate activities among Federal agencies, but also provides a clear path within USDA for the processing of biotechnology research and product requests.

The Deputy Assistant Secretary for Marketing and Inspection Services, Karen Darling, will provide you with specific details regarding the regulatory aspects of the June 26 Federal Register notice.

You also asked that I discuss how the role of the research and regulatory divisions of USDA have been coordinated. I can tell you today that there is a clear understanding within the Department of Agriculture as to the procedures for handling these applications.

On July 14, Secretary Richard E. Lyng issued Secretary's Memorandum 1020-27, formally establishing the Office of Agricultural Biotechnology (OAB). A copy of this document is attached to my testimony and I would request that it be included in the record of today's hearing. This action centralizes the responsibility for implementing and coordinating the Department's policies and procedures pertaining to all facets of agricultural biotechnology in one office, the OAB.

I have initiated steps to obtain a full-time director for OAB. In the meantime, I am functioning as the interim director of OAB, assisted by Dr. Dan Jones of the Food Safety and Inspection Service (FSIS) who is serving as the interim deputy director.

The Department has established a requirement whereby notices of all applications or requests received by USDA for licenses, permits or approvals of agricultural biotechnology products or research falling within the coverage of the June 26 Federal Register notice are to be forwarded to the Director Office of Agricultural Biotechnology. No license, permit, or approval shall be granted by USDA for any agricultural biotechnology product or research without review by the Director of OAB for compliance with Departmental policies and procedures. A copy of the document establishing these procedures is attached to my testimony. The Director of OAB is responsible for maintaining records of research and regulatory activities carried out under the biotechnology authorities of the Secretary.

In order to provide for Departmental coordination between the research and regulatory agencies, we are presently in the process of formally establishing the Committee on Biotechnology in Agriculture (CBA) which will be the policy body for biotechnolgy within USDA. The CBA will be co-chaired by the Assistant Secretary for Marketing and Inspection Services, and the Assistant Secretary for Science and Education. The CBA membership is to be comprised of policy-level representatives of the Agricultural Research Service (ARS), the Cooperative State Research Service (CSRS), the Animal and Plant Health Inspection Service (APHIS), the Food Safety and Inspection Service (FSIS), and the U.S. Forest Service (USFS). The CBA will be of immense value in resolving any conflicts relating to biotechnology applications or requests.

When fully implemented, OAB will perform a staff role for CBA. Whenever OAB believes that proposed agency actions affecting biotechnology require decision-making at the Assistant Secretary level, it will refer such matters on a case-by-case basis to the CBA for resolution by the two Assistant Secretaries.

Mr. Chairman, you asked that we provide a brief description of the principal points of the new USDA policy statement, highlighting those areas which have significantly changed since the December 31, 1984 Federal Register notice. I would summarize the research portion of the statement as follows:

The USDA portion of the "Proposal for a Coordinated Framework for Regulation of Biotechnology" (hereafter referred to as the December 31, 1984 Notice) stated that agriculture and forestry products developed by biotechnology will not differ fundamentally from conventional products and that the existing regulatory framework is adequate to regulate biotechnology.

USDA has both research and regulatory responsiblities for biotechnology activities. This document provides significant new information in both areas. Section II of the USDA Policy describes 1985 Federal Register notices concerning USDA policies and responsibilities for biotechnology. Included in this discussion is an explanation of the assignment of responsibilities within USDA for the oversight of USDA funded research and for the regulation of the products of biotechnology. An understanding of the way in which USDA has divided these responsibilities should prove helpful to those in the private sector seeking review and/or approval of biotechnology applications.

A new section III of the USDA Policy has been added describing USDA's policy for agricultural biotechnology research. USDA published as a companion document in the same Federal Register notice, USDA Guidelines for Biotechnology Research that will closely parallel the NIH Guidelines. The USDA guidelines will be issued under the authority of the Food Security Act of 1985 (Pub. L. 99-198).

This Act amended section 1404(2) of the National Agriculture Research, Extension, and Teaching Policy Act. The amendment gave the Secretary of Agriculture responsibility for establishing "appropriate controls with respect to the development and use of the application of biotechnology to agriculture."

All USDA funded agriculture biotechnology research or research conducted at an entity receiving USDA funds would be subject to the USDA Guidelines for Biotechnology Research unless the specific research project is supported by and subject to the guidelines or regulation of another Federal agency. These Guidelines would encompass all phases of agricultural biotechnology research, i.e. (1) contained laboratory experiments; (2) specialized isolation research (e.g., greenhouse, biotron); and (3) environmental research release (e.g., controlled and segregated field plots). USDA hopes that entities not required to comply with the Guidelines would voluntarily adhere to the requirements. To encourage compliance, USDA proposes to adopt the NIH policy of providing the researchers not required to comply with these Guidelines the opportunity to have their new biotechnology research proposals reviewed by USDA.

Those entities covered by the USDA Guidelines for Biotechnology Research would also be required to comply with any applicable statutes such as those set forth in section IV of the USDA Policy in the June 26 Federal Register notice, and any regulations issued thereunder.

The Office of Agriculture Biotechnology (OAB), described earlier, will have primary responsibility for implementing and coordinating the Department's policies and procedures pertaining to all facets of biotechnology. This includes the conduct of laboratory and field research, experimentation on biotechnology products prior to their commercialization, and oversight of biotechnology in agriculture. The new office will report to the Assistant Secretary for Science and Education. The Assistant Secretary for Science and Education is in the process of establishing an Agriculture Biotechnology Recombinant DNA Advisory Committee (ABRAC) which will continue the responsibilities for agriculture formerly handled by the NIH-RAC during the last 10 years. The CAB shall operate in a manner similar to the Office of Recombinant DNA Activities (ORDA) of the National Institutes of Health. This includes the responsibility for support of the ABRAC and the implementation of the USDA Guidelines for Biotechnology Research. The NIH system is well respected both domestically and worldwide, and has achieved a high degree of efficiency in achieving broad confidence in the safety of new biological research conducted under its requirements.

The OAB also will serve as a focal point for coordinating a National Biological Impact Assessment Program (NBIAP), which is to evaluate and monitor the potential impacts of biotechnological processes and products on safety and the environment.

A new section (V) has been added to the policy statement describing the scientific review mechanisms to be estabished by USDA to assist USDA Agencies in biotechnology research and regulatory decision-making. In the earlier portion of my statement, I described the Committee on Biotechnology in Agriculture and the role which this committee will have.

A detailed summary of comments on the December 31, 1984 Notice and USDA responses appears as section VI. The comments are organized to conform to the form of the December 31, 1984 Notice, with general comments and responses on the USDA regulatory philosophy followed by comments and responses on specific aspects of USDA's regulatory structure.

Mr. Chairman, that concludes my statement. I will be pleased to respond to your questions.

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

July 21, 1986

SUBJECT: Issuances of Licenses, Permits, or Approvals of Agricultural Biotechnology Permits

TO: John Patrick Jordan, Administrator
Cooperative State Research Service

Terry B. Kinney, Administrator
Agricultural Research Service

Bert W. Hawkins, Administrator
Animal and Plant Health Inspection Service

Donald L. Houston, Administrator
Food Safety and Inspection Service

Effective immediately, notices of all applications or requests received by the U.S. Department of Agriculture (USDA) for licenses, permits, or approvals of agricultural biotechnology products or research falling within the coverage of the Federal Register notice of June 26, 1986, entitled "Coordinated Framework for Regulation of Biotechnology," are to be forwarded to the Director, Office of Agricultural Biotechnology, Room 233-W, USDA Administration Building.

Additionally, effective immediately, no license, permit, or approval shall be granted by USDA for any agricultural biotechnology product or research, including those presently being processed, without review by the Director, Office of Agricultural Biotechnology.

This action is taken pursuant to provisions of Secretary's Memorandum 1020-27 of July 14, 1986 (copy attached), and with pertinent Federal Register notices. This memorandum clarifies the memorandum of July 17 which was sent to you.

Orville G. Bentley
ORVILLE G. BENTLEY
Assistant Secretary
Science and Education

ALAN TRACY
Acting Assistant Secretary
Marketing and Inspection Services

cc: Peter Myers, Deputy Secretary
Dan Jones, Office of Agricultural Biotechnology

bcc: Loretta Owens, Dr. Carlson, Ralph Ross, Michael Sauls

UNITED STATES DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D. C. 20250

July 14, 1986

SECRETARY'S MEMORANDUM 1020-27

ESTABLISHMENT OF OFFICE OF AGRICULTURAL BIOTECHNOLOGY

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1 BACKGROUND AND PURPOSE

The U.S. Department of Agriculture (USDA) recognizes that the science of biotechnology holds great promise for improving the quality and availability of our food and fiber supplies, maintaining our position in the international marketplace, and enhancing our natural resources. In order to assure program coordination and operational efficiency, the Office of Agricultural Biotechnology (OAB) is being established.

It is the policy of the USDA to encourage and support the responsible development and utilization of beneficial products of modern biotechnology consistent with the protection of public safety and the environment. The establishment of the Office of Agricultural Biotechnology is deemed to be in the best interests of the public and USDA.

2 ACTIONS ORDERED

Effective immediately, there is hereby established the Office of Agricultural Biotechnology, to be headed by a Director who shall report to the Assistant Secretary for Science and Education. The Office will have primary responsibility for implementing and coordinating the Department's policies and procedures pertaining to all facets of agricultural biotechnology.

3 EXISTING DIRECTIVES

Prior delegations of authority, administrative regulations, and other directives not inconsistent with the provisions of this Memorandum remain in full force and effect.

Richard E. Lyng
SECRETARY OF AGRICULTURE

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Mr. Volkmer. Thank you very much, Dr. Bentley.

At this time I am going to recess. We have a vote on, and we will come back and start again in about 10 to 15 minutes.

[Brief recess.]

Mr. Volkmer. The subcommittee will resume its hearing, and we will now hear from Doctor—or Ms. Darling—"Dr. Darling," for once.

Ms. Darling. That sounds just fine.

Mr. Volkmer. Karen Darling, Deputy Assistant Secretary for Marketing and Inspection Service.

Ms. Darling. Thank you, Mr. Volkmer. It's been a long day. I have learned something. I hope we all have.

I don't want to take much time to talk about some of the regulatory authorities and functions of the Department of Agriculture except for the Animal and Plant Health Inspection Service, because there have certainly been some comments about how we operate at APHIS today. I will go into a little bit of background on how APHIS is presented in the biotech policy statement and how we've stated that it's our perspective that we can regulate new or novel products in the same manner that we have traditional products because of a variety of statutory authority, as so granted.

I think it important to keep in mind as well that in this broad authority that we have under the Plant Pest Act, the Virus Serum Toxin Act, the Plant Quarantine Act and so forth, that we also have our emergency statutes that let us quarantine or stop movement thereof or, as we do so well, kill animal pests or kill plant pests or the exercise that we take to put down a danger to the society.

Certainly, we are not people with the Department of Agriculture or throughout the Government that want to release something into the environment that might be dangerous. And speaking as a regulator and someone also worried about budgets, I don't want to have to spend so much money to put down whatever it is that might cause the problem.

We regulate veterinary biological products, animals and poultry, plant and plant products, meat and poultry products, seeds under—and there are a variety of statutes. Those have been enumerated in the Federal Register from the first Federal Register notice in December 1984.

Under the authority granted by the Virus Serum Toxin Act, the USDA regulates veterinary biological products produced in the United States or imported into the United States. The Food Security Act of 1985 amended the Virus Serum Toxin Act by expanding USDA's authority over such products in several respects. Under the amended statute, it is unlawful to ship or deliver for shipment any worthless, contaminated, dangerous, or harmful biological product intended for use in the treatment of animals anywhere in or from the United States. Previously, intrastate shipments and exports were not subject to that act.

It is also unlawful, subject to certain exemptions, to ship biological products unless they were prepared in compliance with regulations prescribed by the Secretary of Agriculture in an establishment licensed by the Secretary.

The 1985 amendment also extends the Secretary's rulemaking authority and contains new enforcement provisions.

It is taking a bit of time to get everything, every proposal set forward under the Virus Serum Toxin Act because of changing all the regs, all the rules, to reflect both intra and interstate movement as well as import-export.

Currently, we have about 70 establishment licenses out there and about 1,400 product licenses for veterinary biological products. In the context of a biological product, certainly we are concerned about any biological product, whether it be derived from genetic engineering or a traditional method. We're talking a live virus; we're talking moving it. And we do not permit any movement of any biological product without a permit from the USDA. So we have what I feel is good control all the way through the chain. You cannot go from the laboratory to the field without having a permit from the USDA.

Products which are imported into the United States must also be imported under permit issued by the Secretary, and we've issued about a thousand permits under the Virus Serum Toxin Act to perform that function.

Veterinary biological products derived by recombinant DNA techniques that are developed otherwise are listed in the '86 notice. We have—we feel that each product is evaluated individually to determine what will be necessary to establish its purity, safety, potency and efficacy. Scientific considerations may dictate generic areas of concern or for the use of certain tests under specific situations. Special assays, preferably using in vitro methods, may be required for potency and stability determinations. Additional tests may be required to assure safety, especially when live microorganisms are present in the biological product.

The rest of the statement I believe you have before you, and I would like to request that it be submitted into the record. I feel that Dr. Bentley has spelled out very well the coordination that we now have in ~~place and~~ written down and signed off by the Secretary of Agriculture as to the function of the Office of Agricultural Biotechnology which will assure the coordination as well as the inherent cooperation—but will ensure the coordination within the Department of Agriculture both from the research arm and the regulatory arm.

The coordination that we have with other regulatory agencies, like the Environmental Protection Agency, the Food and Drug Administration, have also developed certain processes by which we deal with each other. With the Environmental Protection Agency we correspond back and forth. We ask one another to have an overview of a particular product application that may be in the pipeline, to assure that all the regulatory agencies involved in that particular product feel that we have an efficacious product. I think we've come a long way since we began this process in April 1984. It has certainly been a study in human dynamics as well as looking at the science of this very important process.

I think we've had a pretty long day and I shouldn't say too much more except to say we welcome your questions.

[The prepared statement of Ms. Darling follows:]

UNITED STATES DEPARTMENT OF AGRICULTURE
Statement of
Karen Darling, Deputy Assistant Secretary
Marketing and Inspection Services
Before the
Subcommittee on Investigations and Oversight
Subcommittee on Natural Resources, Agriculture Research and Environment
Subcommittee on Science, Research and Technology
U.S. House of Representatives Committee on Science and Technology
July 23, 1986

Thank you, Mr. Chairman and members of the committee, for the opportunity to present testimony about the Department of Agriculture's policies for regulating biotechnology. I am Karen Darling, Deputy Assistant Secretary for Marketing and Inspection Services. The Assistant Secretary for Marketing and Inspection Services oversees the regulatory activities of the Animal and Plant Health Inspection Service, or APHIS, which includes Veterinary Services and Plant Protection and Quarantine; the Agricultural Marketing Service; and the Food Safety and Inspection Service.

In your July 10, 1986, letter to Secretary Lyng, you requested general and specific testimony in several key areas:

- First, a brief description of the principal points of USDA's June 26, 1986, policy statement on biotechnology, highlighting those areas which have changed since the December 31, 1984, USDA policy statement;

- Second, the adequacy of USDA's authority to review deliberate release proposals submitted to USDA for approval;

- Third, an explanation of how the role of USDA research and regulatory agencies has been coordinated.

USDA's policy statement of June 26, 1986, focuses on new proposals for biotechnology research and regulation. This testimony, in conjunction with the testimony presented by Dr. Bentley, will address your questions about USDA's authorities and interagency coordination.

Before I begin, one further point should be emphasized. Just as the Federal Government has both research agencies and regulatory agencies, the Department of Agriculture has research and regulatory responsibility for biotechnology activities. This distinction is central to an understanding of the coordinated framework for the regulation of biotechnology. The Office of Science and Technology Policy's "Proposal for a Coordinated Framework for Regulation of Biotechnology" of December 1984 was published because the products of new biotechnology were moving, "from the research laboratory to the marketplace." In addition to research agencies such as the National Institutes of Health, and Science and Education of USDA, regulatory agencies such as the Food and Drug Administration, the Environmental Protection Agency, and the Animal and Plant Health Inspection Service (APHIS) of USDA are assuming added responsibility for biotechnology. I will be discussing primarily APHIS' policies and proposals for regulating biotechnology in the marketplace.

The USDA statement of policy for research and regulation of biotechnology applications in agriculture and forestry published on June 26, 1986 (referred to as the June 86 Notice) expands upon the USDA policy statement on biotechnology published in the Federal Register on December 31, 1984 (referred to as the December 84 Notice). It provides new information about policy for agricultural biotechnology research, proposed regulations, and scientific review mechanisms. The concluding section contains a summary of and responses to comments on the December 84 Notice. Part III of the June 86 Notice (51 FR 23351-23393) is devoted entirely to USDA's proposed regulations pursuant to the Federal Plant Pest Act and the Plant Quarantine Act and to proposed guidelines for biotechnology research.

Background

In the December 84 Notice, USDA stated its perspective that agriculture and forestry products developed by biotechnology could be regulated for the protection of the human environment through the administration of existing statutes. USDA also pledged to amend its regulations if the existing regulations proved inadequate. After carefully analyzing the comments on the December 84 Notice, USDA concluded that there was a need to amend the existing regulations. In brief, USDA is responding to the view of the majority of the commenters that USDA should outline additional procedures for reviewing biotechnology submissions by proposing new rules for regulating genetically engineered organisms which are plant pests.

USDA regulates veterinary biological products, animals and poultry, plant and plant products, meat and poultry products, and seeds under a series of statutes described in the matrix published in the Federal Register on November 14, 1985 (50 FR 47174-47195). The statutes most applicable to biotechnology applications are the Virus-Serum Toxin Act (VSTA), the Act of February 2, 1903, the Federal Plant Pest Act (FPPA), the Plant Quarantine Act (PQA), the Federal Seed Act (FSA), the Federal Meat Inspection Act (FMIA), and the Poultry Products Inspection Act (PPIA).

Under the authority granted by the VSTA, USDA regulates veterinary biological products produced in the United States or imported into this country. The Food Security Act of 1985 amended the VSTA by expanding USDA's authority over such products in several respects. Under the amended statute, it is unlawful to ship or deliver for shipment any worthless, contaminated, dangerous, or harmful biological product intended for use in the treatment of animals anywhere in or from the United States. Previously, intrastate shipments and exports were not subject to the Act. It is also unlawful (subject to certain exemptions) to ship biological products unless they were prepared in compliance with regulations prescribed by the Secretary of Agriculture in an establishment licensed by the Secretary. The 1985 amendment also extends the Secretary's rulemaking authority and contains new enforcement provisions.

Currently, there are 70 establishment licenses and 1,403 product licenses for veterinary biological products. APHIS' biologics staff includes a headquarters review staff, a field office inspection staff, and 279 laboratory personnel trained in biologics and diagnostics testing at the National Veterinary Services Laboratories. Those products which are imported into the United States must be imported under a permit issued by the Secretary, and APHIS has issued 1,019 permits under the VSTA.

Veterinary biological products derived by recombinant DNA-techniques or developed from hybridomas have been classified into three broad categories for licensing purposes in the June 86 Notice. This division, which is based on the biological characteristics of the new products and the safety concerns they present, is analogous to the approach used in licensing veterinary biologics produced by other procedures. Each product is evaluated individually to determine what will be necessary to establish its purity, safety, potency, and efficacy. Scientific considerations may dictate generic areas of concern or the use of certain tests for specific situations. Special assays, preferably using in vitro methods, may be required for potency and stability determinations. Additional tests may be required to assure safety, especially when live microorganisms are present in the biological products.

To provide guidance to current or prospective manufacturers employing modern biotechnological methods, USDA in the June 86 Notice has summarized points to consider and data requirements for (1) recombinant DNA-derived products; (2) chemically synthesized antigens; (3) monoclonal antibody products; and (4) master seeds.

Under the authority granted by the FPPA and the PQA, USDA regulates the movement into or within and through the United States of plants, plant products, plant pests, and any product or article which may contain a plant pest at the time of movement. These articles are regulated through a permit system to prevent the introduction, spread, or establishment of plant pests new to or not widely prevalent in the United States.

In Fiscal Year 1985, APHIS' Plant Protection and Quarantine issued 4,840 permits to assure the safe movement of plants, plant products, soil and high risk materials, and nearly 2,000 permits for the continued movement of plant pathogens and noxious weeds. The Plant Protection and Quarantine headquarters staff of 85 specialists includes entomologists, plant pathologists, botanists, mycologists, biostatisticians, biologists, and environmental specialists.

USDA, in Part III of the June 86 Notice, is proposing new regulations pursuant to the FPPA and PQA which would impose restrictions on the "Introduction of Organisms and Products Altered or Produced Through Genetic Engineering Which are Plant Pests or Which There is Reason to Believe are Plant Pests". USDA is confident that organisms altered through genetic engineering will play a major role in increased plant yield and improved plant quality. However, a genetically engineered organism derived from organisms that are plant pests also may present a risk of plant pest introduction. New data will be needed to evaluate permit applications for those organisms which are plant pests or which there is reason to believe are plant pests.

The proposed regulations restrict the "introduction" of certain organisms and products altered or produced through genetic engineering, referred to as "regulated articles." In this context, "introduction" means to move into the United States, to release into the environment, or to move interstate, or any attempt thereat. "Release into the environment" means "use of a regulated article outside the constraints of physical containment that are found in a laboratory, contained greenhouse, or fermenter or other contained structure."

"Regulated article" is defined as any organism or product altered or produced through genetic engineering if the donor organism, recipient organism, or vector or vector agent belongs to a group of organisms designated by the proposed regulations as having plant pests or any organisms or product which USDA determines is a plant pest or which there is reason to believe is a plant pest. Included in the proposed regulations is a list of groups of organisms which are plant pests or contain plant pests. If the donor, vector/vector agent, or recipient of the genetically engineered organism is derived from an organism on the list of organisms containing plant pests, such genetically engineered organism would be deemed a "regulated article."

The proposed regulations require that a person obtain a permit prior to the introduction of a regulated article. In determining whether a permit can be issued for the introduction of a regulated article, USDA will examine the ecological and environmental effects of a release of the genetically engineered organism or product into the environment. The release into the environment of a genetically engineered plant pest would be equivalent to the introduction of a plant pest which is new to and not known to be widely prevalent in the United States, and, therefore, would be subject to regulation under the FPPA and PQA.

Coordination of the Role of USDA Research and Regulatory Agencies

To assist USDA research and regulatory agencies in decision-making, USDA has established a Committee on Biotechnology in Agriculture (CBA) which will be co-chaired by the Assistant Secretary for Science and Education and the Assistant Secretary for Marketing and Inspection Services. The CBA will function both as a policy body in USDA and as a bridge between its research and regulatory structures.

USDA's regulatory agencies' policies and proposals for regulating biotechnology complement Science and Education's research policies and proposed guidelines. The CBA will coordinate the roles of USDA's research and regulatory agencies.

The Office of Agricultural Biotechnology (OAB) established July 14, 1986, will perform a staff role for the CBA. USDA has established a requirement that notices of applications or requests received by USDA for biotechnology licenses, permits, or approval of agricultural biotechnology products or research be forwarded to the Director of the OAB. These written notices will enable the OAB to maintain records of research and regulatory activities carried out under authorities of the USDA. The procedures also require a review by the Director of the OAB for compliance with Departmental policies and procedures before any license, permit, or approval is granted by USDA for any agricultural biotechnology product or research.

I will be pleased to answer any additional questions you may have about USDA's regulatory policy statement and the issues of regulatory authority and interagency coordination you have raised.

Mr. Volkmer. Thank you very much, Ms. Darling.

I would like to start with a few questions here for Dr. Moore.

Under TSCA, if an organism is altered by just the deletion of genetic sequences, such that it exhibits new traits, why wouldn't it be considered a "new" organism?

Dr. Moore. It could be considered new and would be reviewed under TSCA. We certainly would review it and probably put it under an extensive review if the organism that you started with in making the deletion was one that came out of a genus or a species that was held to be pathogenic.

Mr. Volkmer. But if it was nonpathogenic?

Dr. Moore. If it was—if anything that we were proposing to do with these rules in place, if it was nonpathogenic, it would still be subject to our 8(a) notification rule prior to any experiment, but it would not be subject to the intensive review.

Mr. Volkmer. Who makes the decision as to what is pathogenic, and how do they make that decision?

Dr. Moore. Congressman, in a number of instances, classic reference texts are available to define, I think, for the vast majority of circumstances what is pathogenic and what is not. In those instances where the potential regulated individual may have doubt as to whether or not they should be covered or are not covered, our statement strongly encourages that they consult with the agency and maybe prudence would dictate in that circumstance that they presume it's pathogenic, if in doubt, until we tell them it's not.

Mr. Volkmer. Well, because I can envision that you could have an intrageneric transfer between a host that is nonpathogenic but has traits towards pathogenicity and the same type of genera that is pathogenic being placed within that host and could possibly end up with a pathogen, could you not?

Dr. Moore Yes. I think the way something like that could happen is that if indeed you had something that was at low level in a "nonpathogenic" organism and indeed you manipulated its genome such that it starts to express that in far greater quantity, it might then find itself in the circumstances that it now becomes some type of a concern.

We would hope that indeed, since you have to notify us under section 8 prior to going forward, that we would have the opportunity to catch that.

Mr. Volkmer. What if they didn't?

Dr. Moore. Well, if the regulation was in place and they didn't, I guess they would go on with their experiment until we caught them. But I would say if they ignored our regulation, they would probably go along until we caught them as well. Then once caught and if indeed found to have done something wrong, if the regulation was in place——

Mr. Volkmer. If you found it to be pathogenic, then it's in violation of the regulation. Now, prior to the promulgation of your significant-new-use rule, and that is going to be probably, what, 9, 10 months, maybe a year before we have that in place?

Dr. Moore. Typical.

Mr. Volkmer. How do you learn of releases into the environment of existing organisms?

Dr. Moore. Congressman, as we sit here today, with the exception of an individual who may be at the stage of feeling that they want to commence commercial manufacture of an organism, anything that they must do that might fall under the purview of TSCA has to be done on a voluntary basis.

Mr. Volkmer. And if they don't do it, there is no violation?

Dr. Moore. Correct.

Mr. Volkmer. Now, you correct me if I am wrong, but presently under TSCA, substances used for research and development, not for commercial use, are exempt from premanufacturing notification and significant-new-use reporting. Is that correct?

Dr. Moore. That's correct.

Mr. Volkmer. How are you planning to address this problem?

Dr. Moore. That is one of the rulemakings that we are working on to make organisms subject to reporting and not be under the R&D exemption that currently exists.

Mr. Volkmer. Do you have sufficient statutory authority to do that?

Dr. Moore. We're reasonably comfortable that TSCA can get into that.

Mr. Volkmer. All right. What about under TSCA, the testing on fewer than 10 acres without prior review by EPA?

Dr. Moore. Now, there is no reference to either 10 acres of land or one acre of water under TSCA. That's an existing regulation in FIFRA which was for general application to all pesticides. We basically are saying, under TSCA, that you should consult with us too—at a minimum through a notification—and in those instances that we have concerns as it relates to, say, the more extensive organisms, you must report to us.

Mr. Volkmer. I am looking at the Federal Register, June 26, and it says indigenous pathogens, prior notification and review, none if it's under 10 acres.

Dr. Moore. Under TSCA?

Mr. Volkmer. Under TSCA.

Dr. Moore. That would be true because the reference of either acres—either 10 acres or one acre, depending on land or water, is something that is unique to FIFRA in regulation, and there is no reference as it relates to TSCA. There is no regulation in place that speaks to size limitations as to whether you're under it, you don't have to report.

Mr. Volkmer. So you would say they would have to report?

Dr. Moore. Yes, I would say that under TSCA, as far as if you had to report, you would not have a cutoff as a function of size of your planned experiments.

Mr. Volkmer. All right. Now, the guidelines divide genetically engineered organisms into two categories for review under FIFRA. Why was this done, and what is its effect?

Dr. Moore. Basically, one thing that I try to impress upon both the Office of Toxic Substances and the Office of Pesticide Programs; we are promulgating a policy that, given that we were talking about biotechnology in organisms, that I wanted consistency between the two policies unless there was a very convincing reason as to why it should not be consistent. The result of that would be that, as we finally promulgated our June notice, compared to what was our interim policy under FIFRA, we basically went from what was, report everything or at least consult with EPA's Pesticide Program on everything, to a program of consult on everything or at least notify on everything. But indeed we implemented this two-tier review, depending upon the nature of the concern.

I think the practical outcome of the two-tiered review as it relates to pesticides is probably more apparent than is going to be real, because the nature of the organism or the nature of what you are working with and what you propose to do is going to suggest that it causes deleterious effects or else you wouldn't be looking at it as a potential pesticide. So it probably would be captured anyway.

Mr. VOLKMER. Now that we have our new guidelines in place and you're developing your new rule, assuming that those rules would be in place and the guidelines, as we know, are subject to review, but let's say they're all in place and for the first time AGS comes in and says we're developing this ice-minus stuff with gene deletion in a bacteria, existing, nonpathogenic. You're going to treat them differently than you treated them in the fall and spring of this year?

Dr. MOORE. If somebody came in with ice-minus and it was similar, if not identical, to either the AGS or the Lindow request, which was in the genus *Pseudomonas*, we would—they would be subject to the intensive review of the two-part review that we're talking about.

If they came in with a proposed ice-minus type of an experiment which was in a nonpathogenic species, they would get the lower-tier review.

Mr. VOLKMER. So it depends upon the pathogenicity of the product?

Dr. MOORE. Yes.

Mr. VOLKMER. All right. Now, noncommercial R&D is exempt by law, is that correct, not regulation, under TSCA?

Dr. MOORE. Noncommercial would be exempt under section 5, yes.

Mr. VOLKMER. What about——

Dr. MOORE. If a company——

Mr. VOLKMER. That's a minor change in the law?

Dr. MOORE. Right. Congressman, a company that is not deriving any funds from a Federal source and therefore not be impacted by the NIH guidelines or USDA guidelines or something like that, as it sits right now, if they were totally noncommercial and it was nonspesticidal in nature, they would be exempt.

Mr. VOLKMER. After reviewing what is—and the problems with developing guidelines and regulations under TSCA, for any possible biotechnological chemical products, should TSCA be changed to a permitting scheme like FIFRA?

Dr. MOORE. People have raised this previously and said wouldn't it be simple to have a prospective and a positive scheme whereby before you could move forward—akin to FIFRA. In some respects, it would have some intuitive appeal. On the other hand, I think if you did it under TSCA, you would be significantly changing TSCA from the way it was perceived, at least the agency perceives, as to what was intended when it was permitted—when it was enacted.

FIFRA, for example, there's no question, FIFRA is a licensing statute and that is not the intent of TSCA. TSCA is a listing statute and a review mechanism. So it would be a very significant change.

I think that we do have a reasonable chance of being able to adequately control the biotechnology industry under the existing statutes of TSCA. As to whether or not one will be able to do it with the ease and facility that we all might like, I think it's probably best to answer when we get a little bit of experience. We have yet, as we sit here, to receive the first thing under TSCA.

Mr. **Volkmer**. Right. I think we all understand that. But on the other hand, I think some of us again that are laymen, in looking at this, realize that TSCA was developed for a chemical industry which is a lot different from a biotechnology industry where you're going to have possible microbial bacteriological uses that have different traits than chemicals. That's what I think concerns some of us.

Now, OSTP recently commissioned a report on risk assessment methods for biotechnology. It stated in the report that an important requirement in the risk assessment process is detailed knowledge of the environmental and pathogenic characteristics of the modified microorganisms.

Now, will the premanufacturing notice or 8(a) reporting requirements address this?

Dr. **Moore**. We would hope so. We may have to go about it indirectly. Let me take a minute to explain what I mean by that. TSCA is written to not require data upfront to be in the same envelope as the request for consideration to be added to the inventory.

I think what the agency plans to do is to identify the types of information it thinks is required in order to make an informed judgment. If indeed the regulated industry doesn't listen to what that is, or fails to heed what I think is reasonable recommendations, we would then be in a position that we should receive something. Absent such data, I think that we would be required under section 5 to basically sit there and say that, hey, we think we have a presumption here of: may present possible risk of widespread exposure, which is in the statute, and either hold up the granting of the study, or put it under tight requirements by a section 5(e) consent order or something like that. That would probably have the net effect of forcing them to go back and generate the data.

Mr. **Volkmer**. You're going to be able to do that, to show that, without the data?

Dr. **Moore**. We think we can do that much easier with a living microbe than we can with the chemical because of the statement in the statute that speaks to wide exposure. By the very nature of a living organism going out into the environment, I think that's *a priori* evidence that there is potential for wide exposure.

Mr. **Volkmer**. Now, if EPA allows the release of an intergeneric pathogen, let's say, on one acre of land in Florida or anyplace else, the organism goes on the inventory and anyone can release it anywhere unless EPA adopts a significant-new-use rule that requires notification before using it again elsewhere, like 400 acres in my district in Missouri, and 10,000 acres in Kansas. Is that correct?

Dr. MOORE. Yes. Unless we made some type of restriction at the time we allowed something to go on the inventory, once it is on the inventory, it is totally unrestricted. Our intent would be, I think, early on, to work under a presumption that indeed we likely will put it under a 5(e) order where the person who was requesting the PMN and either put it under a—subject it to SNUR to make sure other people can't do things we're preventing the original requester to do, or something similar to that, some type of a restricted inventory category where you cannot do what you are hypothesizing.

Mr. VOLKMER. All right. Now, have you—and I believe you touched this somewhat, and I know Dr. Bentley and Ms. Darling touch this on their end—have you appointed any contact people to work with the USDA on applications where there would be overlapping jurisdictions?

Dr. MOORE. Yes, sir.

Mr. VOLKMER. Those have been appointed?

Dr. MOORE. Yes. We have in every instance—I believe, in every instance—that we've had the nine organisms that have been requested, we have had communication with USDA and indeed have had participation on the part of USDA in their comments as to the appropriateness of what concerns they may have. Even if they didn't have a statutory handle, we want their advice at any rate, and in some instances it is quite appropriate that while we might be having the lead to review the organism in this case, they would point out that, hey, a license—I am sorry—a permit may be required, particularly under the Plant Pest Act.

Mr. VOLKMER. Let's assume that USDA reviews it and they make recommendations that further tests along a certain area, a certain review be done, and your EPA scientists don't agree with that. Now what happens?

Dr. MOORE. All right. Well, I think I can put it in—just generally speaking——

Mr. VOLKMER. Or is that just not going to happen?

Dr. MOORE. Oh, I think it will happen, if it hasn't already happened. I think it will happen, scientists being what they are.

Mr. VOLKMER. They might have some disagreement?

Dr. MOORE. Indeed, there may be disagreement or there may be something that scientist A thought about that scientist B didn't think about, or scientist B thought about and didn't think it was that big a problem, so failed to mention it.

I think when you get a circumstance like that, whether it be EPA, USDA, or whether it's just two scientists in general, we want to sit down and see if—get the two to start to communicate with each other to see why they seem to have a different perspective.

In my experiences, in most instances, the vast majority of circumstances, they both moderate and come to something that is more common to both of them. That is not to say that that happens in all instances. If you end up in an instance—in some instances where there—some scientist says, hey, I understand everything you're trying to tell me but I still think that I might be right, then I guess that's where I get paid for my money for making such a decision as to what do you do in that circumstance.

Mr. VOLKMER. Does a level I review under FIFRA and the TSCA report requirements require less data than level II and PMNs?

Dr. MOORE. Let me make sure I understood your question. A level II review, under either statute, probably would end up having much more data being evaluated than would a level I. That is, it is entirely conceivable, however, that the first piece of correspondence that the agency received could contain the same amount of data and then after we said, wait a minute now, this is going to require more intensive review, we would then ask for additional and then receive that more additional data. If I understood your question right.

Mr. VOLKMER. All right. Now, is—correct me if noncoding regulatory sequence changes are in the lower level of review.

Dr. MOORE. Yes, they would be.

Mr. VOLKMER. Can you tell me why they are?

Dr. MOORE. Well, within the definition, we talk about the exclusion of possibly regulatory sequences, in this case, being—now, based on the judgment of scientific judgment that indeed these types of sequences don't pose any major problems.

Mr. VOLKMER. Now we will start on the other side. We'll start on USDA for a while. Now I was just given a copy of the July 23, 1986, briefing books this morning, Dr. Bentley, of your memorandum, along with Mr. Tracy, in regard to the issuance of license, permits, or approvals of agricultural biotechnology permits. Is that everything that's supposed to be forwarded to the director of the Office of Agricultural Biotechnology? Correct?

Dr. BENTLEY. That's correct. In the case of notice, it's that such applications are there, yes.

Mr. VOLKMER. In other words, if I am out there and I am a firm and I want a license for a new serum or vaccine and I have sent it over to APHIS, they're not to take action on it, they're to send it up to the OAB?

Dr. BENTLEY. Mr. Chairman, we haven't—we wouldn't envision it this way. A matter of—it would undoubtedly proceed with whatever needed to be done, but notice would be made so that there was an opportunity for additional advice, support if needed, to the OAB, and that would be a matter of notices so that we wouldn't want it to be held up in any way.

Mr. VOLKMER. In other words, OAB is just kind of a clearinghouse for notice or somebody knows all what's going on within the agency?

Dr. BENTLEY. Yes, that's partly a part of it, but it would also be a way for alerting others that there might be questions that could be raised and, somewhat along the remarks that Dr. Moore just made, that we would be able to have the person in that office, the director would then—could say, well, that there are questions that might come up as a result of this, say, of a given organism or having to do with prior knowledge of the research, et cetera. And that would be—that would be the purpose of it, yes.

Mr. VOLKMER. How does OAB react with ABRAC?

Dr. BENTLEY. Well, ABRAC would be—it would react in this way; that is, when materials—let us say now that a proposal came in for a research proposal that had release into the environment and was clearly one that needed to—that should be reviewed or at least be given consideration under the guidelines, it would be the one that—it would be the office to get the material to the appropriate chair of the ABRAC to get the process under way. That would be one reaction.

The other reaction might be, in ABRAC, if there was a question that came up in the regulatory—if there was such a question—it could help facilitate getting the material to the ABRAC committee in an expeditious way.

Mr. **Volkmer.** Again going back to the serum or the vaccine, and I am a commercial firm and all my research has been done inhouse without any agency funding, and I have done my laboratory research and now I want to test it out, and I have got a facility owned by my organization. Let's say I am going to use cattle, something for brucellosis; I am going to get rid of brucellosis with this new serum. So I go out and we start shooting, and it turns out, hey, this thing is working. A year later, after I find out that it's working, I sell it off to XYZ corporation over there, and now XYZ is going to—they file an application for a license with APHIS.

Now, can XYZ use those test results in support of the license?

Ms. **Darling.** Mr. Chairman, in support of a license or any application for permit, all data that has been collected or is being collected would be advisable to be submitted at that time. As you know, in APHIS we have all kinds of scientists. They're not necessarily all research scientists, but we've got all kinds of scientists that, while they are notifying the OAB that your XYZ has come in with their application based on your herd, that our staff reviewer——

Mr. **Volkmer.** This is the Volkmer Corporation that did it all, but I have sold it over to XYZ.

Ms. **Darling.** I hope they got a pretty penny for it.

Mr. **Volkmer.** Pardon?

Ms. **Darling.** I hope you got a pretty penny for it and decided to patent it.

Mr. **Volkmer.** Oh, yes, we've got a lot of money now. But you——

Ms. **Darling.** We've been looking for——

Mr. **Volkmer.** You never have heard about this before. We didn't let you know we were doing it.

Ms. **Darling.** Until you wanted to move it inter or intrastate——

Mr. **Volkmer.** No, I didn't tell you that

Ms. **Darling.** Well, you didn't tell us——

Mr. **Volkmer.** I never did tell you.

Ms. **Darling.** But you're going to now because you want to commercially——

Mr. **Volkmer.** No, I am not. XYZ is. I am not.

Ms. **Darling.** Because you're selling to XYZ.

Mr. **Volkmer.** I sold everything. I sold all manufacturing rights and all the information, how to make it and everything else, the process and everything, to XYZ.

Ms. **Darling.** So XYZ is coming to APHIS to say——

Mr. **Volkmer.** Right.

Ms. **Darling** [continuing]. Hey, have we got a product here we want you to look at.

Mr. **Volkmer.** Right.

Ms. DARLING. And I would—probably I am being a little presumptive, but I would presume that all data that has been collected to that point would certainly be admissible to be looked at.

Now, at the same time, we are extremely concerned with the confidential business information to not let out that XYZ really was Volkmer and company's development.

Mr. VOLKMER. Well, that doesn't make any difference. My point—I am trying to get at a point I think you're missing, Ms. Darling, and that is that all the testing was done under the new guidelines, et cetera, as I understand it, and I transported this serum, even intrastate interstate, as I understand it, is supposed to be illegal. I've done all that illegally and you're going to let XYZ use all that information, though. That's what concerns me.

Ms. DARLING. When they submit their application?

Mr. VOLKMER. They submit their application to you and the only test results they show are the ones that we ran and you didn't even know we were doing it.

Ms. DARLING. I see what you're getting at now.

Mr. VOLKMER. Yes.

Ms. DARLING. Yes, because we cannot—we cannot restrict research, or statutorily say this is how you have to run that test before you bring it to us.

Mr. VOLKMER. Right. Now, you can restrict the flow of serum if you find out that, supposing under your new rules you are going to be able to restrict the flow of serum both intra and interstate, but you got to remember my facilities are in a little town and my herd is right outside of town and nobody is going to even know about it. And I didn't even know I was supposed to do it. [Laughter.]

You know, I'm a young guy, a little guy, and I didn't even know I was supposed to do that. See, that's one of the things I want to point out that I——

Ms. DARLING. Yes, I understand.

Mr. VOLKMER [continuing]. This concerns me.

Dr. Bentley, would that concern you, that you're able to use that even though—that information—even though it was illegally done?

Dr. BENTLEY. Yes, it would.

Mr. VOLKMER. And you can't stop it, though?

Ms. DARLING. No.

Mr. VOLKMER. So that's something I think you better look at.

Now, I have submitted that to—XYZ has submitted it to APHIS. When XYZ submitted that data and the application for the license, et cetera, all to APHIS, APHIS sent a notice over to OAB. Correct?

Ms. DARLING. Correct.

Mr. VOLKMER. Now, OAB has got this notice and looking at it and saying, "Hey, that's just another—that's a brucellosis vaccine or eradication serum; that's fine stuff. It doesn't look so bad to us." What will happen as far as the ABRAC is concerned? Will they get into it?

Dr. BENTLEY. This, of course, is plowing some interesting ground. But let me say this, that if this came to the—as it comes to the OAB and as I would envision it—one could ask if it is a genetically modified organism and that's what was used to produce the brucellosis—and I presume that's your——

Mr. VOLKMER. Right.

Dr. Bentley. It was implicit in your comment. It would seem to me that if that had been done without any type of approval, that the original company and now with XYZ buying that and would assume some obligation in this, it would seem, that they would be in violation of the rule that says that organisms, if they use organisms in this, should require—or would require approval at a national level.

Now, then the only thing is, and the question is, whether or not—and this I can't answer for sure whether or not one can say that raises the question about whether or not such licenses as were requested can be granted. I don't know what the legal interpretation is of that, and I don't presume to speak to it.

But it would seem to me that that's the kind of question we have to face and will have to give attention to.

Mr. Volkmer. Dr. Moore, I understand you have a meeting to go to. I have no further questions for you. But if you have any further comments, you may make them, or else you may be excused, however you so desire.

Dr. Moore. I would like the opportunity to go back to the powers of EPA, Mr. Chairman.

Mr. Volkmer. Right. Right. Go back to work. [Laughter.]

Thank you. I still have some questions for Dr. Bentley, though.

The reason I brought that up is it's no different than what we talked about at our first hearings, Dr. Bentley.

Still I don't think you've got them covered yet in your guidelines. I don't care—it's not covered in your rules, and it greatly concerns some of us that what we will see, releases into the environment out here, sometimes it may prove out that all that stuff is fine and it works fine just like it did in the pseudorabies vaccine. But lo and behold, the time will come when it isn't something that works out fine and we have a mess on our hands. That's what concerns me.

Dr. Bentley. Mr. Chairman, let me say one thing that I would like to pursue, and I am speaking now without knowing the restrictions of the law and various things because I am not familiar with all of the ramifications therein.

But it would seem to me that this would be something we might want to consider in rulemaking at a future time, and that would have to be up to APHIS to adjudicate this, whether or not—but it would at least be information on research.

Mr. Volkmer. I think that any data that is going to be used in support of any license, there should be a requirement in the law, or else in the regulations if you don't want a law, at least in the regulations, that the data has been obtained with approval of processes by USDA at least, similar to what EPA does——

Dr. Bentley. Yes.

Mr. Volkmer [continuing]. Especially on genetically engineered products that may be pathogenic or intergeneric types of products.

Dr. Bentley. We would like to look into this application.

Mr. Volkmer. I think you need to look at that.

The other thing I want to go back to is something I still don't fully understand, maybe because sometimes I have a slow osmosis program within my brain, but sometimes it's because it gets confusing, too, out here. That is, when does ABRAC get involved into review of a product that has been genetically engineered?

Dr. **Bentley**. There would be several routes. One would be on request; that is——

Mr. **Volkmer**. Can I ask you this question first?

Dr. **Bentley**. Oh, excuse me. All right.

Mr. **Volkmer**. Does it always?

Dr. **Bentley**. It has——

Mr. **Volkmer**. Will it always?

Dr. **Bentley**. It will not always, because there are exemptions, there are things—protocols as experience is built up, it probably won't be necessary to go through the process. But the process would be, it seems to me, would be initiated under a variety of circumstances. One would be a proposal, let's say, that came from a university or an experiment station where they were going to do some research; they had reviewed it at the IBC level, and wanted—and were releasing it to the environment and wanted a review and approval before going ahead with the research, much as the NIH RAC has done. Those, if necessary, would go to the ABRAC. That would be for their review.

One other situation would be that—again a hypothetical one—let's say that there was a question that came up in connection with a request that was ultimately leading to a license or a permit of some type and it was felt by the judgment of the CBA or the committee or the agency involved that there needed to be a review, that there was a question of review. That would almost fall into the example that you have set here. That could be a request.

Mr. **Volkmer**. Who will make the determination as to whether ABRAC reviews these proposed products or doesn't review them? Who makes that determination?

Dr. **Bentley**. Well, when you get to the final analysis on that, there is one point where we'd say the two Assistant Secretaries that are dealing with the CBA, that's why we have the CBA's, to be a bit of a—to look at questions like that where there are—there is some indecision as to whether it needed to go through the ABRAC. That's why I say there are kind of—there are different levels of this. Some cases it's clear, there's no question about it needs to go to the ABRAC. Sometimes it may not be, and the two assistant secretaries are at the policy level, if it needed to be approved.

Now, most of the time I think those can be settled if one can draw on the experience of the NIH/RAC, many of the times that can be settled by the director of that office because there is a body of information and experience that's used as a protocol that would help us to go by that. So that's how we would generally approach it.

Mr. **Volkmer**. Has the membership on the ABRAC been decided and appointed?

Dr. **Bentley**. The documents creating the ABRAC are in—I think have now all gone through the say of the Secretary's memo. We used that route to establish it, and it's been through review, and the membership has been determined by the agency. That is an internal committee, of course, of agencies, of—the research agencies, the regulatory agencies are members of the CBA.

Mr. **Volkmer**. Would you furnish——

Dr. **Bentley**. Did I miss——

Ms. Darling. ABRAC.

Dr. Bentley. Oh, I am sorry.

Mr. Volkmer. ABRAC.

Dr. Bentley. I am sorry. I was—I——

Mr. Volkmer. You were talking about OAB.

Dr. Bentley. On the CBA, yes.

Mr. Volkmer. CBA.

Dr. Bentley. On the ABRAC we have to make announcements through the Federal Register, establishing that committee, and the process, we now have a statement and the chart, the charter for it has been developed for it. It is now in the process of going through the approval within the department, so it's going to be published in the Federal Register in accordance with the usual procedure for establishing such a public committee.

We should do that. I am not sure of the exact date, but it should be within the very next few days. Then when we get the authorization and the necessary procedures, then we will move ahead with the establishing of the ABRAC.

Mr. Volkmer. Who will ABRAC report to?

Dr. Bentley. It will work through the office of OAB and to the Department, to me.

Mr. Volkmer. Now, the earlier testimony you were hearing, you heard Dr. Mellon talk about some of USDA's program for biotechnology review and regulation. After listening to that and reviewing her testimony, I came to the conclusion that she was saying that basically all USDA is really going to regulate is plant pests.

Ms. Darling. Mind if I go ahead on this one?

Mr. Volkmer. I would like to find out. What about that?

Ms. Darling. Well, Mr. Chairman, you know, I certainly understand their concern. Yes, we regulate plant pests. We are charged with regulating plant pests. Beneficial pests aren't necessarily something that come into an emergency situation by which APHIS needs to regulate beneficial pests. But certainly, we are charged with protecting the American food and fiber system to try to work with, like EPA, to hold down the plant pest population.

I think she is totally wrong in her assessment of how that is viewed, but she will have her opportunity to talk to the Plant Pest Act on the 29th of January in Sacramento, or the 5th of August in this town.

Mr. Volkmer. The 29th of July?

Ms. Darling. 29th of—yes—July, to make her comments and thoughts public, to go into the record on the amendments or proposed amendments to the Plant Pest Act.

Mr. Volkmer. But, in other words, as I understood her point, you can have genetically engineered organisms, products, that could be not necessarily plant pests, but could still be detrimental to society in general. What about those?

Dr. Bentley. Could I speak on that?

Mr. Volkmer. What about that type of——

Dr. Bentley. There are two points. The guidelines, as I understand and interpret it, says that all organisms—that is, genetically modified organisms—are subject to review before release, prepared release into the environment. And we spoke on the TSCA and on FIFRA discussions, and that would apply. And the same thing, therefore, I think that all organisms would be covered in some way in the guidelines, so as far as the organisms are concerned, microorganisms.

Mr. **Volkmer**. All right.

Dr. **Bentley**. Now, with regard to research that would be covered, I didn't read this from my testimony, but in the testimony I point out that the USDA guidelines would encompass all phases of agricultural biotechnology research, and we're talking here of contained laboratory experiments, specialized isolation research, as in greenhouses and biotrons, environmental research releases, whether uncontrolled or in segregated field plots.

All of these are types of things that would be controlled and would be subject to review if they fell under the guidelines, so that we would—and I guess the best way I can describe it is by analogy, would be that many of the kinds of proposals that have gone to the NIH/RAC that relate to agricultural crops or agricultural uses of products would come to Agriculture.

We will handle them in much the same way that has been done over the past few years.

Mr. **Volkmer**. Now, Dr. Bentley, as we have heard previously, there is quite a bit of biotechnology research being done sponsored by USDA.

Dr. **Bentley**. Yes.

Mr. **Volkmer**. Now, some of that undoubtedly is going to come along for releasing some of those genetically engineered organisms at these federally funded institutions, and those will be reviewed and approved by the local IBC. Is that correct or is that incorrect?

Dr. **Bentley**. Yes, that's the first review process, that's right.

Mr. **Volkmer**. Now, let's say the IBC says, "No, I don't think that that product should be released into the environment even on a small field plot," can the investigator or researcher then appeal that to the agency, that decision, or not? Let's say the IBC turns them down on the release. What does he do if the IBC doesn't approve the release?

Dr. **Bentley**. A release into the environment, I believe the rule generally is that all such releases should be referred by the IBC for review to a Federal type of committee such as the ABRAC or the NIH/RAC.

Now, if it wasn't involving release into the environment and the institution turned it down, whether or not an investigator could appeal, I would guess that I wouldn't—I don't know if that's the usual thing, but I would guess that there's always a route or an opportunity for appeal. It would be taken up—I don't know the detail there enough, but I would say that in the case of the release into the environment, that that would be reviewed at the ABRAC level. The IBC would comment on it. I would presume that's the way they would act, but they wouldn't act on it.

Mr. **Volkmer**. Those that have been funded out there—there are quite a few of them—have they been notified of the changes that are taking place as far as release into the environment, what they're going to have to go through before they can go out and field test these products?

Dr. **Bentley**. My answer to that would be yes, because if they were involved before, they were always under the NIH/RAC requirement for release to this, and there is general knowledge that these processes are going on on the prior notice.

Moreover, Mr. Chairman, we have had the opportunity to talk with the leadership in the research programs both internally—and the Agricultural Research Service have been involved in helping us develop these plans that we have, and we have had consultation with the organizations that represent the agricultural experiment station. They used the ESCOP[1] as the specific organization. We have talked with that group. They have a special group that's been in place for about 3 years now in biotechnology. It's an excellent group of people drawn from all across the country involving a broad range of disciplines. So we have had consultations and they know about these, about these developments.

But it won't seem too different to the scientists who have been doing research, or the agricultural experiment stations.

Mr. **Volkmer**. Because they have been working under the NIH/RAC?

Dr. **Bentley**. Yes. They will see that as similar, and we will—we stress that repeatedly.

Mr. **Volkmer**. OK. I want to get back to when I was going over the question of licensing that brucellosis vaccine or serum. Ms. Darling, I would appreciate it if you would talk to Mr. Tracy about it and take it up with your scientists and as a matter of policy more, I guess, even than scientific fact. I have said this before, that somewhere if you can't; I would like to know that you can't; if you can't provide by rule that before data would be available for use for licensing of a product, that any commercial institution applying would have to certify that the applicable research guidelines and all steps had been taken and followed before that data could be used. I think that's one way we could prevent somebody—at least to have something to try to prevent people from doing things that are unauthorized in the commercial sector outside the institutional sector.

Ms. **Darling**. Absolutely. And, Mr. Volkmer, I understand that XYZ corporation——

Mr. **Volkmer**. Right.

Ms. **Darling** [continuing]. Would be called upon to develop all data and any data received, say, on another flock or from another company could serve as background, certainly. But they would have to comply with data requirements as submitted for a particular product by XYZ.

Mr. **Volkmer**. OK. The question we've had before, Dr. Bentley, and especially when we've had Mr.Tracy up—I think it would apply to him more than yourself—the question of confidential business information. I know that in discussing this before with Mr. Tracy, we had the question—not the question, but the problem, according to Mr. Tracy, of that information being subject to review by a RAC—ABRAC at that time; it wasn't the ABRAC, it was a different——

Dr. **Bentley**. Yes.

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[1] Experiment Station Committee on Organization and Policy.

Mr. **Volkmer**. Because they didn't know whether or not that confidential information would remain within the USDA now and in fact could only APHIS personnel review that type of information? Now, will ABRAC still not review those, that information? Will that confidential type of proprietary information still be withheld from the ABRAC?

Dr. **Bentley**. Again, my understanding—I am not thoroughly familiar with all the requirements of the CBI; all I know is that it's an important element and needs to be given serious consideration. I know that.

I would say, in our guidelines, as we talked about it, there are provisions that have been worked out that—where material can be properly redacted so that it can be used. The company itself has to identify what is really confidential information as a part of their submission. As I understand that, in FDA and other places that is done. And therefore, that would be the part that you would have to honor.

We think that there can be processes in drawing on the experience of the NIH/RAC to use the kind of process and procedures that were used there to govern—to protect CBI elements so that we can take a look at—so they can be reviewed.

Now, I would suspect that sometimes maybe that isn't possible. But it would seem to me that that could be worked out, and we are in the process of discussing that within our Department right now about that question. I must defer to the regulatory people that have had long experience with CBI to find out how to do it, what procedures or what guidelines must be followed.

On the other hand, I think we hope that there can be a way found so that we can handle this question of confidential business information to satisfy the requirements of the department, of the law itself, and certainly of the client, the person that's sending in material.

Mr. **Volkmer**. Well, what concerns me a little bit and, I think, some others that I have talked to—the gentleman from Iowa, Mr. Bedell—all the people who are going to be looking at it are USDA people.

Dr. **Bentley**. That's right.

Mr. **Volkmer**. And why are APHIS people able to look at something and keep it confidential and maybe somebody else within a different agency of USDA not being able to do that? That's what's hard for some of us to understand.

And if you're going to say that once this information—let's say there is a filing for an application with APHIS for a certain product that has been genetically engineered, and the company puts down the type of product and its intended use as confidential—now you say you're going to notify the OAB and notify the CBA about what's coming, but they can't put on that notice what it is and what it's going to be used for? What good is the notice?

Dr. **Bentley**. Right.

Mr. **Volkmer**. Do you understand where I am——

Dr. **Bentley**. Yes, I understand what you're speaking of.

Mr. **Volkmer**. Now, if they can put it on there and send a memo up to OMB or CBA yourself and the other assistant, if they can't do that, surely you can give that same information to people that are serving on ABRAC. Aren't the ABRAC people—are they going to be USDA people, mostly?

Dr. **Bentley**. I think there are two parts. The one part that is all—we are all, as I understand it, all Federal employees are under CBI. We're under the same restriction or the same covenants as anyone else would have. So therefore, it can be reviewed under the—at the CBA. It could be looked at at the CBA.

On the ABRAC, there will be people on the ABRAC because it is a public committee who will not be non-USDA or non-Federal appointees. There might be people from on the ABRAC that will be from other agencies of the Federal Government that assist us. We will want to give that consideration.

The system, as I understand it, that has been used in the NIH/RAC, that the non-Federal appointees have to sign an agreement on this that binds them to the same kind of obligation for that particular time as under CBI.

Now, again we are going to want to get—learn from others in this case as to how to proceed in terms of techniques and the way we will handle it. But that would be the way we would do it.

We would also hope, though, that in many cases, as many cases as possible, that the individual that is submitting a proposal of that type would indicate that with the removal of certain kinds of information that this matter, they wouldn't have objection to others reading it. We have such a thing, I think, in the Calgene proposal that is being reviewed, that the people of Calgene are not concerned at sharing most of their proposal—and probably more than we need to share for the information we need—except certain parts of it will be removed. They name the pages, and those will have to be removed. But that wouldn't necessarily mean that you couldn't be—it couldn't be reviewed. It would be the specific gene sequence or the specific section they're moving, which would not necessarily change—change the proposal.

I think this is a difficult thing for us to work out, but we're going to work at it, and we certainly have to give serious thought to the obligations of APHIS and FSIS within our department, within the agency, and the same would be true, say, if we were cooperative on looking at a venture that came to EPA that had the same requirements. I don't know exactly how you do this and all the details, but I think there are enough guidelines for us that we can work it out.

Mr. **Volkmer**. Well, I think you should be able to work it out, Dr. Bentley. Again, sometimes maybe we don't see the forest for the trees—and I am speaking of myself, not you, now—but some things, maybe some things that are obvious to some of us on the outside may not be truly obvious.

But you know, Monsanto made the application to EPA for an experimental use permit for releasing some bacteria that had been genetically engineered on some corn, in the State of Missouri, in fact, to be released in my district. That was reviewed by a committee just like ABRAC.

Dr. **Bentley**. Yes.

Mr. **Volkmer**. From what you are telling me, though, if Monsanto would make an application to USDA for an end product that had to do with something agricultural, which they probably will somewhere along the line——

Dr. **Bentley**. Yes.

Mr. **Volkmer** [continuing]. That right now you would have reservations about subjecting that information to an ABRAC review if it had CBI in it. Now, I know that when a CBA or EPA advisory committee, Science Advisory Committee, looked at it, that's why it's hard for me to understand what's the difference between the two.

Dr. **Bentley**. Mr. Chairman, this is a meeting to exchange views of individuals. I would not say that—we would proceed with such a review in our department. What the problems we might have to go through to get there, that's the part I don't know exactly. But if you wanted to know my view, we would try to proceed in exactly the same way as was done in EPA as far as having a review if it was called for in the ABRAC. In fact, we have to find a way to do that, and I just am an optimist, I always feel we can work these things out.

Mr. **Volkmer**. Well, as I said before, I don't think my problem is with you as much as it is with Mr. Tracy.

Mr. **Bentley**. Well, I would like to——

Mr. **Volkmer**. He's not here to defend himself. I mean, that's my——

Dr. **Bentley**. I would like to speak for Mr. Tracy and Karen Darling and the Department of Agriculture. We will find a way, and we may have some internal questions to resolve, but I think we can resolve that. I say I am speaking for myself and the way I would approach it. I just know that can be resolved because we have had staff members from our universities and from the Department of Agriculture that have served on the NIH/RAC for several years and helped, in fact, create that. They've served on the EPA advisory committee as well.

Mr. **Volkmer**. Ms. Darling, can you explain on the plant pest, under the Plant Pest Act, how you can regulate an organism that may pose a risk as being a plant pest when it's not proven to be one yet?

Ms. **Darling**. I think by your statement itself, Mr. Chairman, it might pose.

Mr. **Volkmer**. But doesn't the statutory language say that it has to be before you can regulate it, and that's statutory law? That's what—I may be wrong. I think—do you disagree with my interpretation of the law?

[No response.]

Mr. **Volkmer**. In other words, if you have an interpretation, you're of the opinion if you have an interpretation that it could cause injury, then it would be designated a plant pest even though it hasn't been proven to do so?

Ms. **Darling**. If it could, if the potential is there.

Mr. **Volkmer**. All right. Have you ever done that? Have you ever, to your knowledge, on the basis that one that could, not one that has?

Ms. **Darling**. Yes, I think probably numerous times.

Mr. **Volkmer**. OK. Now, our final question, Dr. Bentley or Ms. Darling, whoever, have you all appointed your contact people—I suppose you have—to work with EPA on applications where there's an overlapping—possible overlapping jurisdiction?

Ms. **Darling**. Yes.

Dr. BENTLEY. As we get the OAB functional, that will be one of their very important tasks.

Mr. VOLKMER. That will be part of the OAB?

Dr. BENTLEY. Yes. It would be—the OAB provides us not only as a functional office but a staff person that can devote time to being sure that these kinds of arrangements can be made, communications person, just to facilitate who makes the call, who makes the contact.

Ms. DARLING. And aside from that, we already have two parent committees in APHIS that contact—over contact with EPA.

Mr. VOLKMER. All right. You have had some already contact with them, like on the Monsanto application.

Ms. DARLING. We certainly did.

Mr. VOLKMER. You made recommendations and it appears that those have pretty well worked out between EPA and USDA?

Ms. DARLING. In that case, EPA had requested the USDA to review that application, which we so did. The EPA asked for a second of our own opinion, and we also tendered that, and it was their decision that it was a product that was clearly within those jurisdictions of the EPA. But appropriately, as set out in the policy framework, they have asked us for our review. We will, in turn, do the same thing on anything that looks like a cross-jurisdiction. Of course, we do have those.

Mr. VOLKMER. OK.

Does the gentleman from California have any questions?

Mr. PACKARD. Thank you, Mr. Chairman.

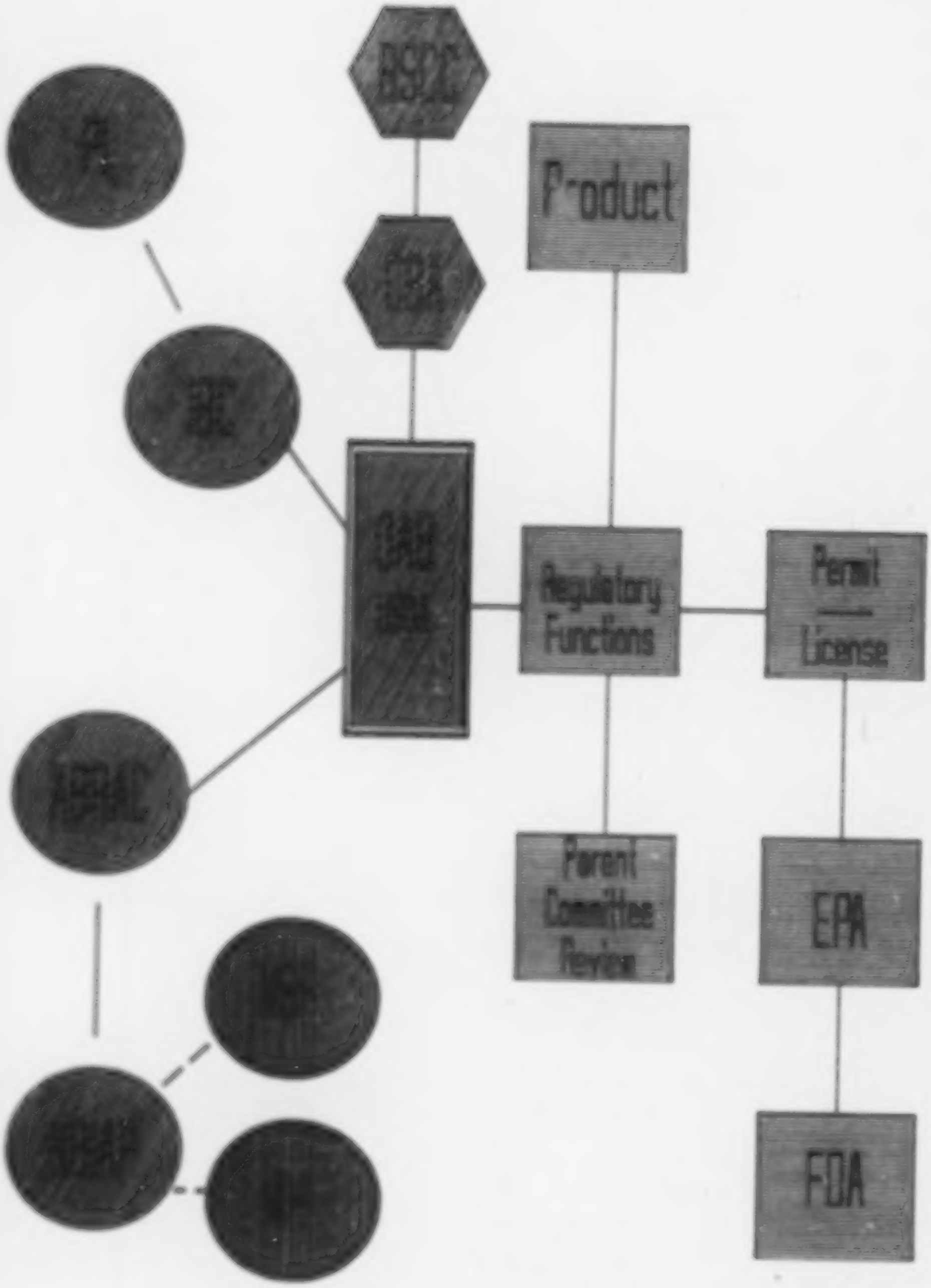
I have four questions. May I just request for the record—repeatedly the witnesses have indicated a flow—even to the extent of perhaps a flowchart of one authority and one agency to another and within the agencies, one function or of one committee to another. I think it would be helpful if the committee could actually get, if it's available, the flowchart of the review process.

Dr. BENTLEY. Yes.

Mr. PACKARD. What you have, I think we ought to have in terms of—because several questions have been in relation to how the different committees will review and from there where it goes. Any comment?

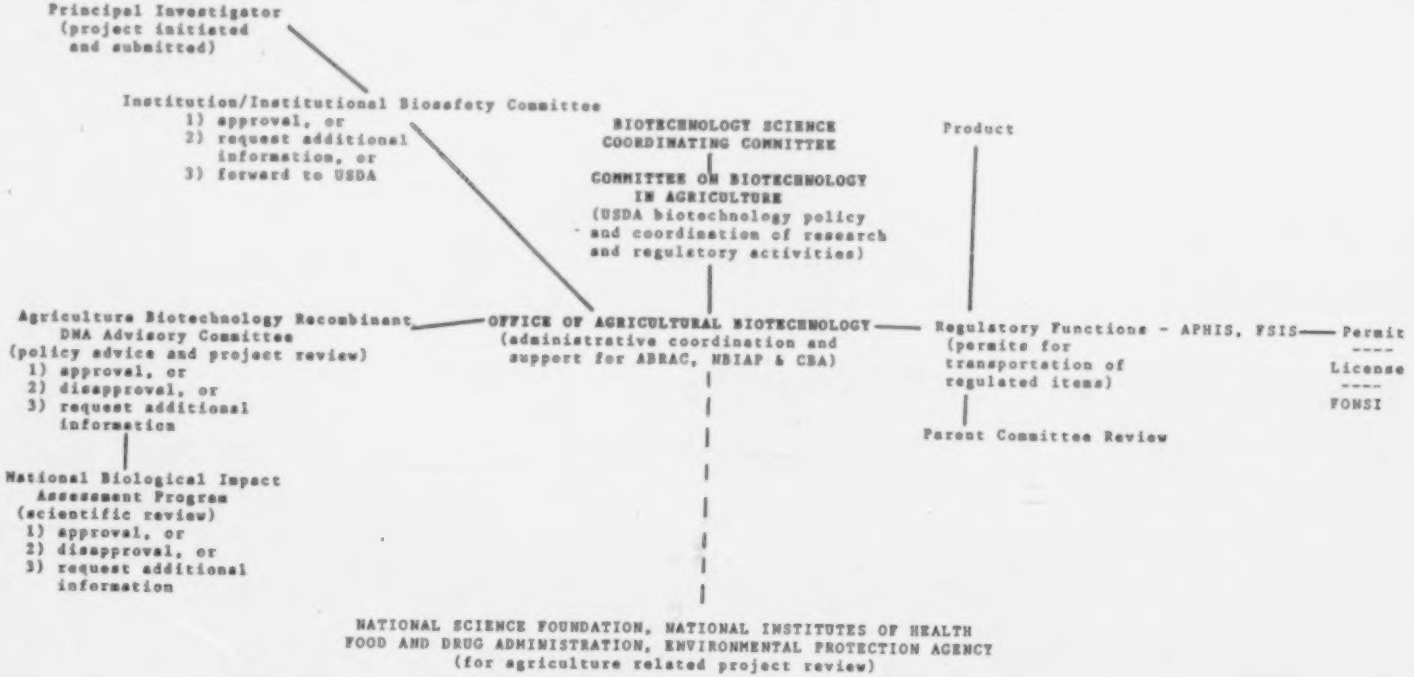
Dr. BENTLEY. Mr. Packard, we have such a sheet. We have it laid out, a chart. We've taken pictures of it and so on. We would like to just, if I may, we would be glad to submit that to the committee. We would like to review it once more. We made a lot of changes and a lot of things in the last ten days or so that we would like to look at. But we have a chart for you.

[Information follows:]


BSCC
Product
Regulatory Functions
Permit
License
Parent Committee Review
EPA
FDA

USDA ENVIRONMENTAL AND SAFETY APPROVAL PROCESS FOR AGRICULTURAL BIOTECHNOLOGY RESEARCH

(As Mandated by the Agricultural Biotechnology Research Guidelines)


Principal Investigator
(project initiated
and submitted)
Institution/Institutional Biosafety Committee
1) approval, or
2) request additional information, or
3) forward to USDA
BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE
COMMITTEE ON BIOTECHNOLOGY IN AGRICULTURE
(USDA biotechnology policy and coordination of research and regulatory activities)
Product
Agriculture Biotechnology Recombinant DNA Advisory Committee
(policy advice and project review)
1) approval, or
2) disapproval, or
3) request additional information
OFFICE OF AGRICULTURAL BIOTECHNOLOGY
(administrative coordination and support for ABRAC, NBIAP & CBA)
Regulatory Functions - APHIS, FSIS
(permits for transportation of regulated items)
Permit
License
FONSI
Parent Committee Review
National Biological Impact Assessment Program
(scientific review)
1) approval, or
2) disapproval, or
3) request additional information
NATIONAL SCIENCE FOUNDATION, NATIONAL INSTITUTES OF HEALTH
FOOD AND DRUG ADMINISTRATION, ENVIRONMENTAL PROTECTION AGENCY
(for agriculture related project review)

July 23, 1986

Mr. PACKARD. Thank you. Under the Noxious Weed Act, would you be kind enough to explain how the statute can be used to require prerelease review of genetically engineered plants? Doesn't the regulation of such a weed require a rule and public notice and public hearings? Examples of weeds regulated under the act clearly show that a plant has had to spread considerably before the rule could be promulgated. I was wondering if you could explain how that proceeds.

Ms. DARLING. Mr. Packard, I understand we're not utilizing the Noxious Weed Act in the context of the proposals of the policy statement, but more under the Plant Quarantine Act, Plant Pest Act rather than the Noxious Weed Act.

Mr. PACKARD. So the procedure then, would it be changed under the new guidelines?

Ms. DARLING. From the Noxious Weed Act?

Mr. PACKARD. Yes.

Ms. DARLING. Not that I envision.

Mr. PACKARD. OK. Also, we have not discussed, to my knowledge, penalties. Again, I apologize for not being able to be here during the full hearing. The penalties for violation: I would be interested in knowing how penalties will be applied, whether they will be applied to institutions or researchers, individuals, or both, and whether they will be consistent with the penalties of other agencies and so forth. Would you wish to respond?

Dr. BENTLEY. I think that is really at least two major parts to the answer to that. Let me treat the one that has to do with research. The one, for an agency that does not comply with these rules, let's say, a university that's getting funding from—part of all of its funding for a project from USDA, we can withhold funding of program—withhold the allocation of funds. That is the major hammer that you do have, and this can be, having been in the university most of my career, I know that that can be applied and it can be applied in times when it becomes rather critical. We hold up the release of funding. You usually hope you never come to that kind of a situation, but that would be, in the final analysis, one of the ways.

Now, there are other penalties, specific penalties that have to do with license and permits which I don't—I am not familiar with, and so I would turn to Karen.

Ms. DARLING. Actually, in breaking a statute under the APHIS, under the APHIS statutes, we have civil penalties, criminal penalties, and administrative penalties. Administrative action, we could withdraw a permit if a permit had been activated. We have civil fines. You can always turn it to the Justice Department for a criminal investigation.

Mr. PACKARD. Are they—are most of the penalties planned or considered directed at the institution, or do the researchers themselves become involved in penalties?

Ms. DARLING. I would envision whoever makes the application.

Dr. BENTLEY. In a case of research, I think since most of the funds are institutional, it would be to the institution. That is, if a State agricultural experiment station has a fund of money that comes to that institution. In a case of individuals, I am not positive of that, but the mechanisms that I have ever been familiar with, it went via the institution to the investigator.

There haven't been too many of those, but that's the way it's been applied. Because when the private investigator—"private investigator," I didn't mean that—the research investigator develops a proposal, it has to have gone through the university system; it has to have some institutional commitment or else it wouldn't be a proposal. That would only handle it. So the institution is the one you have to get back to in that case.

Now, an individual disobeying of the law, of some law that pertains thereto, such as fraud or other kinds of statements, then it goes to the individual.

Mr. **Packard**. So an individual, if an individual is actually in violation at one institution, that individual would not be able to move to another institution and still continue the funding on a project? It's not—it couldn't transfer the funds?

Dr. **Bentley**. No. There have been some wonderfully creative people that have done some things like that in their life, and I am always amazed at it when they can do it. But normally, that would not be the case. So I am—because there is too much institutional communication and agency communications to do this.

We would hope that the violation part would be on the minor side, that we would be mostly dealing with that, and I am sure that's the way you mean it, too.

Mr. **Packard**. Yes.

Ms. **Darling**. Mr. Packard, my counsel just advises that submitting a false application could be a felony crime.

Mr. **Packard**. I see. How do your regulations apply to laboratory work that is not conducted by institutions, done by private firms, perhaps even without Federal funding?

Dr. **Bentley**. Well, the guidelines say that it does not necessarily directly apply to people that are funding their own research or carried on in the private sector. However, if that moves to—that involves a plant pest, for example, that that does; those guidelines apply. It doesn't make any difference whether it's public or private. Or if they go to release a genetically modified material into the environment in a planned way, in a controlled way, that applies.

For conducting research on a modified product in a laboratory, it is not a requirement but we have the feeling that many people would like to work on a voluntary basis. That's work that has been very effective in the NIH situation where people sought the additional confirmation and additional confidence in their own decisions on the way they handle their products, they sought as much advice and help as they could. I think that from our conversations that we've had with some of the major biotech firms, large and small, that they are going to be seeking the same thing in the case of the USDA.

Mr. **Packard**. How would you normally be aware of experimentation being done by a small private firm that has not done business through your agency before? How would you know that they were doing any research?

Ms. **Darling**. We don't.

Mr. **Packard**. You don't.

Dr. **Bentley**. We wouldn't know—most of—what I am saying is that I think if they have research of this type and they know about the general guidelines relative to the handling of modified R&D in DNA-modified material, they would more than likely come to the agency and ask whether or not it would be useful for them to participate, to get a review. We would encourage them to be linked to an IBC, an Institutional Biotechnology Committee or a Biosafety Committee, and many of them are. They have their own, or they are linked to another. So it would be in the linkages.

Now, there is no legal requirement that I know that I could think of at the moment that says they're violating the law if they don't do that.

Ms. **Darling**. We aren't going to have backyard people doing it.

Dr. **Bentley**. No.

Perhaps I could add one thing more to that, Mr. Packard. There is a matter of liability insurance and all of the things that go with an individual in the private sector, and if most of those call for prudent action on the part of the individual in protecting against any problems. One of the steps in prudent action would be to seek advice and counsel in areas where there is uncertainty about such matters as biotechnology. As I understand it, this is one of the questions that is coming up: what is the nature of the risk? I am talking about the civil risks that a corporation or a company would have like that, and I think one of the things that they might do to enhance their position would be to assure that they complied with generally accepted rules.

Mr. **Packard**. Thank you. Getting back to the Noxious Weed Act, it has been pointed out to me that it is included in your guidelines as one of the acts that—well, let me read it,

> For informational purposes, footnote one has been included to inform persons that the introduction into the United States of organisms that have been altered or produced through genetic engineering may be subject to other regulations that have been promulgated under the Federal Plant Pest Act, the Plant Quarantine Act, and the Federal Noxious Weed Act.

But you will primarily deal through the Quarantine Act, as I understood your comment before.

Dr. **Bentley**. Well, for the introduction of materials, that's correct. They would be subject to that whether it says biotechnology or not—there are those kinds of rules and those are well in place.

I was just reminded of an additional point that many—much of the research that is going to be developed, whether it's in the private sector or the public sector or in the small unit, you really do have a communications system out here. That is pretty—that is very perceptive in this area, and it's very likely that somebody will do this just on their own, that they might, but that's very unlikely. There is the whole system of the agricultural experiment stations, what we were referring to the—as we work together, we would know about that. There is a system of extension workers that are working, interacting with agencies where they might get help. Then, of course, there is always the whole matter of the legal system as far as violation of various rules.

Mr. **Packard**. Thank you.

Do you have any response to that, Ms. Darling?

Ms. **Darling**. Pardon me?

Mr. **Packard**. Did you have any response that you wanted to add?

Ms. **Darling**. No, just that I was trying to find just where you were here.

Mr. **Packard**. Well, it's on page——

Ms. **Darling**. 23353?

Mr. **Packard**. 23353.

Ms. **Darling**. Where we talk about regulations are only being proposed under——

Mr. **Packard**. Yes.

Ms. **Darling** [continuing]. The Plant Quarantine Act and the Plant Pest Act, that at this time we're not proposing any changes to the Noxious Weed Act.

Mr. **Packard**. Thank you.

That's all I have, Mr. Chairman.

Ms. **Darling**. And, my goodness, I hope nobody genetically engineers a new noxious weed.

Mr. **Packard**. I would agree.

Mr. **Volkmer**. Thank you very much, Ms. Darling, Dr. Bentley. I appreciate the time you spent here today. It's been very helpful, and I am sure that when this all washes out, it will all work out. I appreciate your continued cooperation. Thank you very much.

Ms. **Darling**. Thank you for your patience.

Mr. **Volkmer**. Before we go to the final panel, I do have a few questions, and I would ask Dr. Mary Ann Danello, from Food and Drug Administration, Dr. William Gartland, from National Institutes of Health, and Mr. Edward Baier, from OSHA, to come to the table. I have a very few questions I would like to ask, about one each.

Dr. Gartland, what is the status or outcome, if there has been a final determination on NIH's investigation into the field testing of the pseudorabies vaccine by the principal investigators of Baylor College of Medicine in Texas?

Dr. **Gartland**. Yes, Mr. Chairman. The NIH Director, Dr. Wyngaarden appointed an NIH committee on May 7 to look into that situation of the alleged violation of the NIH Guidelines. The committee has had several meetings. They have received a report from both Baylor and Texas A&M, and they anticipate having a final report out by the middle or the end of September.

Two of the major issues they have got to look into are, first of all, was this vaccine—did this vaccine—consist of recombinant DNA molecules; and second, was there release into the environment involved in this situation.

Mr. **Volkmer**. We will be interested in a final determination. I will be honest with you, we will have to contact Dr. Wyngaarden, I guess, to get a—we can write him a letter and ask him that we be furnished with——[4]

Dr. **Gartland**. We would be happy to——

Mr. **Volkmer** [continuing]. A copy of the final determination, whatever it may be.

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[4] See appendix 9, p. 256.

The other question I have for you, Dr. Gartland. I don't know if you have had an opportunity to review the Federal Register of June 26, 1986, with regard to the guidelines of USDA. On page 23390, we have a start of, under section 404: Functions of Institutional Biosafety Committees. And if you haven't had an opportunity to review those, I would appreciate if you would, and then maybe get back to us in writing.

My question basically is: Do you think the IBC's, as they are presently structured—in other words, that basically—are they not structured basically with volunteers from the institutions?

Dr. GARTLAND. Correct. They are usually—they are usually employees of the institution plus several members who are not affiliated with the institution.

Mr. VOLKMER. But they are of nonpaying status, is that correct?

Dr. GARTLAND. Correct.

Mr. VOLKMER. Presently structured, can they handle all that responsibility that USDA has delegated to them? I would appreciate it, if you haven't reviewed it—have you reviewed it?

Dr. GARTLAND. I have not reviewed that section in detail.

Mr. VOLKMER. All right. I would appreciate it if you would review that and then get back to us, because I have some reservations about, "The IBC review shall include assessment of containment levels required by these Guidelines for proposed agricultural research, and assessment of facilities, procedures, practices, training, and expertise of research personnel. The IBC shall notify principal investigators of results of review, set containment levels specified in subpart 'blank' three, review periodically agricultural biotechnology research to ensure that requirements of the Guidelines are being fulfilled, and adopt emergency plans covering accidental releases." Then we keep going.

Dr. GARTLAND. OK, I will be happy to review that.

Mr. VOLKMER. I would appreciate it, and I would like to have your comment in writing. And also, in that comment, as to whether or not these guidelines for the IBC's are in accord with the role that the NIH/RAC had defined for IBC's, when you first developed the IBC, if it follows that or not.

Dr. GARTLAND. OK. I will be happy to do it.[5]

Mr. VOLKMER. Thank you.

Dr. Danello, does FDA have any concerns about the export of unapproved biological products, such as vaccines for humans, that have been produced by recombinant DNA?

Dr. DANELLO. As you realize, the FDA has been in support of recent legislation which would loosen some of our export provisions, to allow the export of unapproved drugs, the theory being that there may be some drugs, such as vaccines that you mentioned, which would not be used here in the United States, such as malaria, a malaria vaccine, but that would be quite useful in Third World countries.

But the simple answer to your question is that, no, we do not have those concerns at the moment, again realizing that we treat biotechnology-produced vaccines the way we would any other conventionally produced vaccine.

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[5] See appendix 7, p. 248.

Mr. VOLKMER. The fact that they haven't gone through any FDA approval process would not give you any concern?

Dr. DANELLO. Yes, currently they cannot be exported unless they are approved.

Mr. VOLKMER. OK.

Dr. Baier, or Mr. Baier—OSHA has in the past proposed workplace chemicals regulation by measuring exposure within the workplace. Is that correct?

Mr. BAIER. That's correct.

Mr. VOLKMER. EPA has testified that any release—any release—of genetically engineered organisms constitutes significant potential exposure. Now, how will OSHA set standards governing workplace exposure if any exposure can be viewed as significant in the biotechnology field?

Mr. BAIER. Well, for the Agency to develop any standard, we must demonstrate significant risk. EPA primarily has reasonable/unreasonable risk. EPA, calling it significant, may or may not, through the rulemaking process, be determined to be significant risk. I don't know if that makes sense.

Mr. VOLKMER. What you are telling me is that significant to EPA may be one thing but different—have a different meaning to OSHA?

Mr. BAIER. The Supreme Court defined it for us under the benzene standard.

Mr. VOLKMER. All right.

Mr. BAIER. And we must go through the rulemaking process, following the Administrative Procedures Act, and then make a determination.

Mr. VOLKMER. So will you be following the benzene significant-exposure definition basically, or will you——

Mr. BAIER. We really have no choice. When the Supreme Court made that decision, we abide by it.

Mr. VOLKMER. Then you will follow that as far as exposure to biotechnology products?

Mr. BAIER. Yes, that's correct. You see, we neither issue permits nor license any of these, but our fundamental concern is to protect the worker.

Mr. VOLKMER. I understand that.

Mr. BAIER. Yes.

Mr. VOLKMER. And the question is: What is significant exposure to the worker?

Mr. BAIER. That would be decided through the rulemaking process, and that is defined.

Mr. VOLKMER. All right. We will have to review that ourselves to see if we think we should make some changes in it.

Mr. BAIER. Good. Good.

Mr. VOLKMER. All right. OK, I think that's all the questions I have of you three, and I appreciate——

Mr. BAIER. That was a good question.

Mr. VOLKMER. Thank you. [Laughter.]

The next question: Was it worth waiting all day for? That's the followup.

Mr. BAIER. That's right. [Laughter.]

Thank you, sir.

Mr. VOLKMER. Thank you. You all don't have to stay if you don't want to, for the last witness.

Our final witness today is Mr. Richard Godown, Industrial Biotechnology Association, IBA.

STATEMENT OF RICHARD GODOWN, INDUSTRIAL BIOTECHNOLOGY ASSOCIATION, ACCOMPANIED BY DR. ALAN GOLDHAMMER

Mr. GODOWN. Mr. Chairman, I am accompanied today by Dr. Alan Goldhammer, who is our technical adviser and scientific adviser. Dr. Goldhammer has his Ph.D. in biochemistry, and we are here as a team to attempt to, first, deliver some testimony and then respond to your questions. So, if I may, I have a short statement for the record.

IBA welcomes the opportunity to appear again before the subcommittees as the administration's coordinated framework for biotechnology regulation is considered. We hope that, with the clarification of this Federal agency oversight role, the benefits from products of the new cell fusion and recombinant DNA technologies can be delivered to society in both a safe and timely manner.

We would point out that while these two techniques are relatively new, the vast majority of the products generated from the new biotechnology will not differ greatly from existing products which have been widely used in the pharmaceutical and food processing industries, in agriculture, and in waste management. There is a long history of both workplace and environmental safety associated with traditional biotechnology activities.

IBA is examining the present statement on biotechnology regulatory policy and intends to comment on its implications to the individual agencies, and we would be pleased to make these comments available to the subcommittees when the comments are completed.

In order to judge the adequacy of the proposed policies, we, IBA, formulated a series of questions that we believe reflect not only industry's concerns but also the concerns of the public at large. It must be strongly noted that there must be public trust in the regulatory process, and at the same time it is critical that the regulatory process be firmly based on the best scientific knowledge available so that regulations are commensurate with risks. Industry is cognizant of this, and we have attempted to address these concerns at every opportunity.

If the following questions can be answered in the affirmative, IBA believes that this regulatory policy will meet the needs of both industry and the public, and the questions are:

Are the jurisdictional responsibilities for the agencies clearly established?

Do the agencies have the necessary statutory authority to implement and enforce the coordinated framework?

Is the best available science being utilized in the regulatory process?

Do the proposed regulations take into account past scientific experience?

Are there provisions for oversight of products about which there is uncertainty?

Does the proposed policy focus on the review of products as opposed to processses—we have heard that one.

And, will the confidential business information be adequately protected?

Let me discuss very briefly each of those questions. First, are the jurisdictional responsibilities for the agencies clearly established? It's important that the regulatory jurisdiction over particular products be clarified so that there is no uncertainty about the responsibility of each agency. And while a second agency may be called in to deal with the special concern regarding a product, lead agency jurisdiction should be clearly established. This process has worked well in the past and should be continued as new biotechnology products are regulated. Chart I in the policy statement clearly points out how jurisdictional questions will be resolved. IBA believes that this scheme will provide a basis to route products to the regulatory agency with the appropriate authority and expertise.

Do the agencies have the necessary statutory authority to implement and enforce the coordinated framework? Each of the regulatory agencies involved in the coordinated framework has statutory authority to regulate particular classes of products in particular ways. All of the regulations and policy statements contained in the coordinated framework appear to be consistent with the authority granted to these agencies by the Congress.

IBA is aware that one commenter has raised a concern about USDA authority under the Plant Pest Act to conduct pre-release reviews of genetically engineered organisms to determine whether they are suspected plant pests. The two components of this question are: Does the prohibition against unpermitted movement of a plant pest only appear when the organism originates in another state or country, or does it also apply to novel organisms created in a laboratory?

The second part of the question is: Given the statutory definition of a plant pest, does USDA have authority to require prerelease review of known plant pests only or are suspected plant pests also subject to review?

The Plant Pest Act is broadly written to enable USDA to protect American agriculture from plant pests that cannot be controlled under the Plant Quarantine Act. This broad congressional intent is reflected in both the statute itself and its legislative history. The law explicitly gives USDA the power to promulgate regulations imposing any conditions upon the movement of plant pests as is deemed necessary to prevent the introduction or dissemination of plant pests. The Department even has explicit authority to conduct warrantless searches of entrances into the United States and interstate travelers if probable cause exists.

In answer to the first question, USDA's authority to prevent the introduction, spread, or establishment of plant pests appears to be broad enough to permit regulation of novel organisms created in a laboratory for release into the environment. Since the deliberate release of a genetically engineered organism may result in the interstate movement of that organism, it is appropriate for USDA to treat such a deliberate release as if it is an interstate movement.

This interpretation is consistent with the legislative history of the Plant Pest Act, which indicates that it should be construed broadly so as to enable USDA to protect American agriculture from plant pests.

With respect to the second question, it seems plain that before USDA can require a permit or otherwise control the movement of an organism, it must first determine whether a suspected plant pest is in fact a plant pest. USDA's authority to make this determination is integral to its ability to regulate plant pests as required in the statute. We believe that only an obtuse interpretation of the statute would lead one to conclude that USDA does not have the authority to determine whether or not a novel organism is a plant pest.

The third question is: Is the best available science being utilized? Here we note that FDA has—as an agency—has been able to call upon the research capability at the FDA Office of Biologics to assist in clarifying uncertainties. IBA believes that the establishment of the biotechnology Science Advisory Committee at EPA and the Committee on Biotechnology and Agriculture at USDA will prove useful resources to refine and improve the regulatory process at those agencies.

The next question: Do the proposed regulations take into account past scientific experience? One of the major goals of any regulatory framework is that it should take advantage of experience gained with past use and regulation of similar products. As we have stated previously, many of the new biotechnology products will raise no different health or environmental concerns than their traditionally produced counterparts.

A significant amount of experience has been gained through the use of classical mutation and selection techniques, both for microorganisms used for fermentation purposes as well as those used in the environment. The NIH Recombinant DNA Advisory Committee similarly has developed information showing that the suspicion of risk associated with most recombinant organisms is unfounded.

Throughout these various studies, it is clear that there are concerns about the use of pathogens in either contained or environmental settings. We would point out that pathogenic microorganisms will be regulated by this new policy. Data about the ability of similar microorganisms to exchange genetic material has been accumulating. It is clear that this is a common occurrence within a given genus, and as long as pathogens are not involved, regulatory concerns, we submit, should be minimal.

However, much less is known about intergeneric transfer of genetic information. NIH has compiled a list of those microorganisms that do engage in intergeneric gene transfer, and this experience should be used by regulatory agencies to develop a possible list of exemptions, as appropriate. Since recombinant DNA technologies can create microorganisms with traits that they would not normally acquire, it is prudent that regulatory agencies provide some oversight in this area.

Next question: Are there provisions for oversight of those products about which there is uncertainty? Any regulatory regime should have provisions that allow agencies to review products which could have unreasonably adverse effects. IBA believes that the central issue here concerns the field research involving novel genetically engineered organisms.

Several commentators have pointed to the unknown ecological consequences regarding the release of such organisms. We have in the past taken the position that small-scale field tests of genetically engineered organisms do not pose unreasonable risk and can be successfully managed. We support a prudent policy of Government oversight at this research stage and believe that as data are acquired, this requirement can be eased.

Next question: Does the proposed policy focus on the review of products as opposed to processes? IBA has commented at length on the need for product-driven regulatory review. The risk assessment process leading to product approval should be driven by the nature of the product and its intended use. Many products of the new biotechnology will be no different from existing products and should not be treated differently. Process-oriented reviews can have adverse impacts on innovative technologies.

The seventh question is: Will confidential business information be adequately protected? We believe that all of the agencies have adequate authority to protect confidential business information.

In summary, then, Mr. Chairman, we believe that the answers to each of the seven questions is, "Yes," and that this framework is adequate to ensure that the health and environment are protected. We believe that jurisdiction is clear, that the framework is appropriately stringent, and that the articulated policies are enforceable.

I would add this, that we are looking at here—what we're looking at is not a perfect document, that is, the coordinated framework. We are, rather, looking at a compromise intended to coordinate the application of existing and future regulations. We find it workable and welcome. Like products of committee activity, undoubtedly it will need some further clarification based on experience. If there is this much controversy and difference of opinion over a regulatory framework based on existing statutes, imagine the situation which would apply with a brandnew statute or significant substantive amendment to existing law.

We sense it is the desire of the subcommittees conducting this joint hearing, and certainly the desire of industry and the chairman, that biotechnology proceed in an expeditious manner consistent with the public health and safety. We believe that the guidelines will permit that.

[The prepared statement of Mr. Godown follows:]

TESTIMONY OF THE INDUSTRIAL BIOTECHNOLOGY ASSOCIATION BEFORE THE SUBCOMMITTEES ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT; SCIENCE, RESEARCH AND TECHNOLOGY; AND INVESTIGATIONS AND OVERSIGHT OF THE COMMITTEE ON SCIENCE AND TECHNOLOGY HOUSE OF REPRESENTATIVES

July 23, 1986

Mr. Chairman, IBA welcomes the opportunity to appear again before these subcommittees as the Administration's coordinated framework for biotechnology regulation is considered. IBA hopes that with the clarification of this federal agency oversight role, the benefits from products of the new cell fusion and recombinant DNA technologies can be delivered to society in both a safe and timely manner.

We would point out that while these two techniques are relatively new, the vast majority of the products generated from the new biotechnology will not differ greatly from existing products which have been widely used in the pharmaceutical and food processing industries, in agriculture, and in waste management. There is a long history of both workplace and environmental safety associated with traditional biotechnology activities.

From the outset, IBA recognized that biotechnology products would be subjected to government regulation by appropriate agencies. The Association has been an active participant along with other members of the public as governmental agencies have been formulating regulatory policy, a process that was initiated some three years ago. Last year we commented at length on the initial proposal from the Administration that was outlined in the December 1984 Federal Register.

IBA is examining the present statement on biotechnology regulatory policy (51 FR 23302) and intends to comment on its implications. We would be pleased to make these comments available to the subcommittees when they are completed.

In order to judge the adequacy of the proposed policies, IBA has formulated a series of questions that we believe reflect not only industry's concerns but also concerns of the public-at-large. It must be strongly noted that there must be public trust in the regulatory process. At the same time it is critical that the regulatory process be firmly based on the best scientific knowledge available so that regulations are commensurate with risks. Industry is cognizant of this and we have attempted to address these concerns at every opportunity.

Beyond federal regulatory efforts, IBA and its members are actively involved in cooperative efforts to develop standards, specifications, terminology, and test methods so as to assure quality and enhance the safety of biotechnology products. We believe that our participation in the newly created biotechnology committee of the American Society for Testing and Materials demonstrates our commitment to good science, environmental safeguards, and industry self-regulation.

If the following questions can be answered in the affirmative, IBA believes that this regulatory policy will meet the needs of both industry and the public.

1. Are the jurisdictional responsibilities for the agencies clearly established?

2. Do the agencies have the necessary statutory authority to implement and enforce the coordinated framework?

3. Is the best available science being utilized in the regulatory process?

4. Do the proposed regulations take into account past scientific experience?

5. Are there provisions for oversight of products about which there is uncertainty?

6. Does the proposed policy focus on the review of products as opposed to processes?

7. Will confidential business information be adequately protected?

1. Are the jurisdictional responsibilities for the agencies clearly established?

It is important that the regulatory jurisdiction over particular products be clarified so that there is no uncertainty about responsibilities of each agency. While a second agency may be called in to deal with a special concern regarding a product, lead agency jurisdiction should be clearly established. This process has worked well in the past and should be continued as new biotechnology products are regulated. Chart I in the policy statement (51 *FR* 23304) clearly points out how jurisdictional questions will be resolved. IBA believes that this scheme will provide a basis to route products to the regulatory agency with the appropriate authority and expertise.

2. Do the agencies have the necessary statutory authority to implement and enforce the coordinated framework?

Each of the regulatory agencies involved in the coordinated framework has statutory authority to regulate particular classes of products in particular ways. All of the regulations and policy statements contained in the coordinated framework appear to be consistent with the authority granted to these agencies by Congress.

IBA is aware that one commentator has raised a concern about USDA authority under the Plant Pest Act to conduct pre-release reviews of genetically engineered organisms are suspected plant pests. The two components of this question are:

(1) Does the prohibition against unpermitted movement of a plant pest only apply when the organism originates in another state or country, or does it also apply to novel organisms created in a laboratory?

(2) Given the statutory definition of a "plant pest," does USDA have authority to require pre-release review of known plant pests only, or are suspected plant pests also subject to review?

The Plant Pest Act is broadly written to enable USDA to protect American agriculture from plant pests that cannot be controlled under the Plant Quarantine Act. This broad congressional intent is reflected in both the statute itself and its legislative history. The law explicitly gives USDA the power to promulgate regulations imposing any conditions upon the movement of plant pests as is deemed necessary to prevent the introduction or dissemination of plant pests. [7 U.S.C. 150ee.] The Department even has explicit authority to conduct warrantless searches of entrants into the United States and interstate travelers if probable cause exists. [7 U.S.C. 150ff.]

In answer to the first question, USDA's authority to prevent the introduction, spread, or establishment of plant pests appears to be broad enough to permit regulation of novel organisms created in the laboratory for release into the environment. Since the deliberate release of a genetically engineered organism may result in the interstate movement of that organism, it is appropriate for USDA to treat such a deliberate release as if it is an interstate movement. This interpretation is consistent with the legislative history of the Plant Pest Act, which indicates that it should be construed broadly so as to enable USDA to protect American agriculture from plant pests.

With respect to the second question, it seems plain that before USDA can require a permit or otherwise control the movement of an organism, it must first determine whether a suspected plant pest is in fact a plant pest. USDA's authority to make this determination is integral to its ability to regulate plant pests as required in the statute. We believe that only an obtuse interpretation of the statute could lead one to conclude that USDA does not have the authority to determine whether a novel organism is a plant pest.

IBA therefore believes that USDA has adequate authority to conduct pre-release reviews of organisms that are likely to be plant pests.

3. Is the best available science being utilized?

The use of the best available science in the regulatory decision process protects the public interest and instills confidence. This has been the experience at the FDA and that agency has been able to call upon the research capacity at the FDA Office of Biologics to assist in clarifying uncertainties. IBA believes that the establishment of a Biotechnology Science Advisory Committee at EPA and the Committee on Biotechnology in Agriculture at USDA will prove useful resources to refine and improve the regulatory process at those agencies.

IBA believes that by putting the best available science into the risk assessment process, the public will be assured that biotechnology products will be thoroughly evaluated prior to introduction.

4. Do the proposed regulations take into account past scientific experience?

One of the major goals of any regulatory framework is that it should take advantage of experience gained with past use and regulation of similar products. As we stated previously, many of the new biotechnology products will raise no different health and environmental concerns than their traditionally produced counterparts. A significant amount of experience has been gained through the use of classical mutation and selection techniques, both for microorganisms used for fermentation purposes as well as those used in the environment. The National Institutes of Health Recombinant DNA Advisory Committee, similarly, has developed information showing that the suspicion of risk associated with most recombinant organisms is unfounded.

Throughout these various studies, it is clear that there are concerns about the use of pathogens in either contained or environmental settings. We would point out that pathogenic microorganisms will be regulated by this new policy.

Data about the ability of similar microorganisms to exchange genetic material has been accumulating . It is clear that this is a common occurrence within a given genus and as long as pathogens are not involved, regulatory concerns should be minimal.

However, much less is known about inter-generic transfer of genetic information. NIH has compiled a list of those microorganisms that do engage in inter-generic gene transfer and this experience should be used by regulatory agencies to develop a possible list of exemptions as appropriate. Since recombinant

DNA technologies can create microorganisms with traits they could not normally acquire, it is prudent that regulatory agencies provide some oversight in this area. IBA believes that many if not all of these constructs can be well described and should present few or no health or environmental problems.

5. Are there provisions for oversight of those products about which there is uncertainty?

Any regulatory regime should have provisions that allow agencies to review products which could have unreasonable adverse effects. IBA believes that the central issue here concerns the field research involving novel genetically engineered organisms. Several commentators have pointed to the unknown ecological consequences regarding the release of such organisms. We have in the past taken the position that small-scale field tests of genetically engineered organisms do not pose unreasonable risk and can be successfully managed. IBA supports a prudent policy of governmental oversight at this research stage and believes that as data are acquired this requirement can be eased.

It is clear from this policy statement that the regulatory agencies have addressed this point. We do not believe that any biotechnology products about which there is uncertainty will be overlooked.

6. Does the proposed policy focus on the review of products as opposed to processes?

IBA has commented at length on the need for product-driven regulatory review. The risk assessment process leading to product approval should be driven by the nature of the product and its intended use. Many products of the new biotechnology will be no different from existing products and should not be treated differently. Process-oriented reviews can have adverse impacts upon innovative technologies.

FDA, the agency with the most experience in biotechnology product review, has successfully employed this method of regulatory review. Our reading of this policy statement indicates that both EPA and USDA will follow suit.

7. Will confidential business information be adequately protected?

IBA believes that all of the agencies have adequate authority to protect confidential business information.

In summary, IBA believes that the answers to each of the seven questions is yes and that this framework is adequate to ensure that health and the environment are protected. We believe that jurisdiction is clear, that the framework is appropriately stringent, and that the articulated policies are enforceable. We thank you for the invitation to present our views and would offer to answer any questions that the subcommittee members have.

Mr. **Volkmer**. Thank you very much. I appreciate your testimony. I have a few questions, and I suppose the first one, Dr. Goldhammer maybe will want to answer, I don't know. Either one.

But are the definitions as to micro-organisms to be regulated, to the extent that they're going to be regulated or reviewed, clear enough to allow the industry to determine into which category their products are going to fall?

Dr. **Goldhammer**. Yes; we have had no difficulty in either determining which agency would review a given product or within a particular agency, under what section of the statute. We really, unlike what the chairman this morning had expressed, have found no difficulty in interpreting the regulatory documents.

Mr. **Volkmer**. I am quite interested in that because you are on the side of the ones who are going to have to decide that.

The present EPA regulatory policy states that under section 8(a) of TSCA, the Agency will issue a rule requiring companies to submit general information on the environmental uses of microorganisms that are subject to TSCA, but not otherwise subject to notification requirements. Now, is it clear to the industry exactly what information should be supplied? Are you going to have to go to EPA to find that out?

Dr. **Goldhammer**. This, as I understand it—and I talked with EPA 2 weeks ago on trying to get an idea, as you did earlier in asking Dr. Moore—what the timeframe was for the promulgation of all the rules. In addition, on the timeframe question, I don't think that they have decided yet on what types of information they expect the companies to supply under 8(a). I think that this is going to be a process that will, if it hasn't already started taking place, will start taking place very soon, and we certainly, when it appears in the Federal Register, will have comments on it.

Mr. **Volkmer**. Fine. Do you see any problems with voluntary compliance by industry and the minimal, let's say, of 1 year before we get the rule?

Dr. **Goldhammer**. Well, we have already seen this in the agriculture area. We have two companies, both of which are our member companies, that voluntarily went into APHIS to have genetically engineered plants reviewed. They have received approvals for those, and I can say that they have been in the ground now almost a month with no adverse environmental effects that have been noted.

I have also heard from APHIS there have been, I believe, at least 10 or 12 other applications from one or more companies that are presently being reviewed there, and these are all being done on a voluntary basis.

Mr. **Volkmer**. You don't see just because—we have none yet—but just because it may be a new chemical——

Dr. **Goldhammer**. Right.

Mr. **Volkmer** [continuing]. Some biological form, through genetic engineering, you don't see any problems until the new rules go into effect on that side either?

Dr. **Goldhammer**. No. We have asked this of our regulatory committees, if people would think that this might be some difficulty, and the only area that we can see people coming into the Agency in advance of some of these rules coming out would be for fermentation products. Right now, to our determination, there are no contemplated environmental releases, that would be subject to TSCA, in the pipeline.

Mr. VOLKMER. All right.

Mr. GODOWN. If I might add, Mr. Chairman, that it is manifestly in the best interest of the companies involved to have as much approval on record as they can, and so they are really anxious to come before an agency who can give them some sort of green light.

Mr. VOLKMER. Now, presently TSCA's reporting requirements do not apply to small businesses.

Dr. GOLDHAMMER. To section 8(a)?

Mr. VOLKMER. Yes.

Dr. GOLDHAMMER. We surveyed this. It was indicated this point may come up, and I would refer you to the final rule which was published November 16, 1984, in the Federal Register. The Agency does leave itself an out here, and if I might just quote from this in two areas.

First, the Agency has concluded that it is inappropriate to exempt a company from section 8(a) if the firm produces a subject chemical in substantial quantities. High volume—and this is speaking to chemicals here—"High volume of chemical production reflects a greater potential for environmental release. Production data, therefore, would be valuable to EPA as a measure of chemical exposure risk."

And then in a following paragraph, the Agency states, "EPA also has the authority to change the general exemption standards contained in this rule in appropriate cases when Agency access to necessary information is blocked by the exemption."

Now, I would gather, taking those two paragraphs together, that in their proposed 8(a) rule, that they may in fact alter the small-business exemption to address the problem that you raise. But again, we will have to wait for the rulemaking process.

Mr. VOLKMER. Do you see any adverse impact on industry if they do change that definition or, let's say, allow no exemption under TSCA for biotechnologically developed new products—as they call them, new products? What if they say, "No exemption"?

Dr. GOLDHAMMER. Well, 8(a) is not to really regulate new products per se but the use of products that fall outside of that category. The BSCC has also recognized this, and I believe one of the subpanels that they have set up is chartered to acquire data on all of the microorganisms that we currently have in commerce or have been released into the environment.

We support the concept of 8(a) as a reporting requirement, because I think the agency can strongly profit in developing a data base on what has gone out there.

Mr. VOLKMER. From your testimony, Mr. Godown, I assume that you have no concerns about the sharing of jurisdiction between EPA and USDA; you don't foresee any problems with duplication or anything like that?

Mr. GODOWN. I would think the lead agency concept will carry them through, and we don't anticipate any major difficulties.

Mr. VOLKMER. All right. In other words, you're looking more for concurrent review than any type of sequential thing, basically?

Mr. GODOWN. Yes, sir.

Mr. **Volkmer**. Hoping for that at least?

Mr. **Godown**. Yes, sir, whatever it takes.

Mr. **Volkmer**. All right.

I have no further questions. I want to thank you very much. I appreciate your being here again. You have been very helpful, and as we go through this, we appreciate everybody's testimony. So thank you very much.

Mr. **Godown**. Thank you, Mr. Chairman.

[Whereupon, at 4:28 p.m., the subcommittees were adjourned.]

APPENDIX 1

SEP 3 1986

From: Dr. David T. Kingsbury
Assistant Director for Biological, Behavioral
and Social Sciences
National Science Foundation

Answers to follow-up questions from the July 23, 1986 hearing before the Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources and the Environment, and the Subcommittee on Science, Research and Technology of the U. S. House of Representatives, Committee on Science and Technology.

Q 1. According to the statement announcing its formation, the BSCC is intended to serve merely as a coordinating forum on biotechnology policy issues. In your testimony, you state that the BSCC has "primary responsibility for the scientific questions that arise in the future." How do you reconcile these two views of the BSCC's responsibilities.

-- How can the BSCC decide scientific questions, given the limited range of scientific disciplines represented on the BSCC?

A. The statement establishing the BSCC does not state that is to serve merely as a forum on biotechnology policy issues. In the notice establishing the BSCC (FR 50, No. 220, p. 47176) it states:

> "Accordingly, a FCCSET committee is being established to coordinate science issues related to research and commercial applications of biotechnology, the Biotechnology Science Coordinating Committee (BSCC).
>
> "The charter of the BSCC clearly establishes its interagency coordination role. The purposes of the BSCC are to:
>
> > 'Serve as a coordinating forum for addressing scientific problems, sharing information and developing consensus;
> >
> > 'Promote consistency in the development of Federal agencies' review procedures and assessments;
> >
> > 'Facilitate continuing cooperation among Federal agencies on emerging scientific issues; and
> >
> > 'Identify gaps in scientific knowledge."

It is my opinion that this statement is consistent with my comments regarding the role of the BSCC.

As the statement above suggests, the BSCC is not the body which "decides scientific questions," but is in place to coordinate the information gathered by the agencies' staff scientists and advisory personnel. The BSCC works through a series of subcommittees which represent a broad range of disciplines and agencies.

Q 2. You state that the BSCC will clarify questions of agency jurisdiction, questions of data submission requirements, as well as develop "mechanisms of full implementation" of the agencies' regulation. Under what authority will the BSCC go beyond its coordination function and engage in these traditional agency and interagency functions?

A. The quote from the Federal Register notice which announced the establishment of the BSCC, provided to question 1 above, outlines the stated goal for the BSCC in this area. The committee functions under the authority of its charter from FCCSET as well as a Memorandum of Understanding signed by each member of the BSCC. That agreement pledged cooperation and willingness to participate in this type of coordination activity by each of the agencies involved.

Q 3. In your testimony, you state that the BSCC's major responsibility is to "review the appropriateness of the scientific basis of existing regulation" and to recommend statutory changes, if necessary. How can you reconcile this ambitious assumption of regulatory oversight with your other statements that BSCC merely coordinates?

-- Now that the agency policy statements have been published, what role will BSCC play in monitoring the implementation of these policies?

A. As part of its regular proceedings the BSCC will be discussing the pending applications being reviewed by each of the agencies. This will allow the BSCC to assess the changing technology as it is being developed, and to anticipate the new directions the research and products may be following. One of the stated roles for the BSCC is to participate in discussions regarding new kinds of product applications that come into an agency and means whereby the agency feels confident in handling them. When the technology takes a new direction or a direction which may not be covered by one of the existing statues the BSCC members will recognize that change and will be in the position to recommend action to remedy the situation. This will be a scientific judgement, well within the role of the BSCC.

The BSCC will fulfill its charter and the spirit of the Memorandum of Understanding. This will place the BSCC in the position of coordinating and monitoring the developments and pending applications and to encourage interagency sharing of staff in the review process.

Q 4. What role will the BSCC have in ensuring that reviews by more than one agency of applications to release organisms into the environment will have comparable rigor?

A. As outlined in the previous question, it is the intent of the BSCC to monitor the progress of various applications and to review the nature of the applications and of the review process. Where appropriate we will encourage the sharing of staff between the agencies. This review process will allow each agency to understand the nature of the reviews done by the other agencies and to adopt those elements which might strengthen their review process. We have no statutory authority to demand that an agency follow a prescribed procedure but the force of peer pressure by the other members of the committee will assist in encouraging agency adoption of appropriate review procedures.

Q 5. How can the BSCC ensure that the agencies' policies remain coordinated while each agency is promulgating its own rules.

A. It is our intention that the scientific questions associated with any rulemaking will be discussed with the BSCC. In addition it is the role of the Domestic Policy Council Working Group on Biotechnology to continue to monitor and coordinate the various agency statements and rulemaking.

Q 6. At the July 9 open meeting of the BSCC, you stated that the BSCC had contacted various scientific associations for advice in developing the definitions offered by the federal policy statement. Which groups had input into shaping of the scientific principles embodied in the policy statement?

A. On page 39 of the proceedings of the July 9, 1986 open meeting I made the following statement:

> "In fact, we did consult a variety of people, but the fact is that, as I said then and as Mr. Cohrssen has just repeated, these were done interactively with the agencies. The agencies, in many cases, consulted their scientific bodies and, again, if one wants to get that information, then the agency representatives are the appropriate place to go."

I would like to reiterate that the definitions were not a function of the BSCC but of the individual agencies coordinated by the BSCC. The BSCC officially, as a body, relied on the agency contacts for advice in the formal sense. Individually, BSCC members spoke with a variety of individuals with knowledge in this area. Several scientific societies such as the American Society for Microbiology had their annual meetings in Washington and many scientists were available for informal discussions.

Q 7. The BSCC definitions subject "intergeneric organism" and "pathogens", but not other types of genetically-engineered organisms, to full review. What are the scientific and policy grounds for this approach?

-- What are the essential differences in data requirements between an "abbreviated" review and a "full" review?

A. The BSCC definitions themselves do not have regulatory impact and, therefore, do not in themselves establish the nature of review for a product. In so far as the individual agencies have applied their versions of the definitions, they have regulatory impact. The recommendations for the handling of deletions and intrageneric gene transfers and for the exemption for the fully characterized regulatory sequences were derived from a similar recommendation made to the NIH RAC several years ago and incorporated into the NIH guidelines. Other elements of the guidelines, such as the genetic exchanger list, were not incorporated at this time, subject to further review.

The differences between the review processes are outlined in detail in the EPA policy section of the June 26, 1986 notice. They may be found on pages 23321 and 23322.

Q 8. You stated at the hearing that, "There is a level of review for gene-deletions. But it is not the full review, ...it's notification review. It's not a premanufacturing notification." What does the term "notification review" mean in this context?

A. This review will be carried out under the provisions of TSCA, section 8(a) which authorizes EPA to collect a broad range of data, including information on chemical composition and structure, production and use of the material. This process is described on page 23331 of the June 26, 1986 notice.

Q 9. At a hearing on June 5, 1986 on biotechnology, a microbiologist testified that deleting genetic material from a microorganism has, in one case, changed the plant host range of that microorganism. If that is a possibility, why do the BSCC guidelines exempt certain gene-deleted organisms from "full" review?

A. There is no scientific evidence that deleting genetic information from a nonpathogenic microorganism will transform that organism into a pathogen. This position was reiterated by the President of the American Society for Microbiology when he testified on June 5, 1986. The suggestion that the "host range" of a microorganism is changed implies that it is a parasite and that it would be considered a plant pest and therefore be reviewed as a pathogen in the first place. The exemption from "full" review applies only to organisms which are not already included in the "full" review category for other reasons. Deletion mutants are one of the most common forms of naturally occurring mutations. They are used by geneticists for a wide variety of studies because, unlike point mutations, they cannot revert to the wild-type form and no longer have the property for which they have been selected. Deletions offer a distinct advantage for environmental applications because they are absolutely stable and therefore predictable.

Q 10. As you noted, the agency that funds research will review and approve research protocols with assistance from NIH, NSF, or USDA's Division for Science and Education. How will this review system be implemented on a case by case basis?

A. Each government agency which sponsors research involving recombinant DNA molecules has established a policy regarding the adherence to a set of rDNA guidelines. At present each agency uses the NIH guidelines which specify the nature of what type of research fall within the requirements for review by the RAC. At present the Director, NIH has determined that there are other committees, such as those at NSF and USDA which may be more appropriate for the review of certain proposals than the RAC. He has determined that individual funding agencies are the most appropriate place for determination of the best committee for review. Therefore, at present, each funding agency is working from a standard set of guidelines and making individual determinations which review committee should be contacted to examine a specific proposal. Once that committee has been provided with the necessary materials it will be in direct contact with the investigator to obtain any additional information that may be necessary. This is a very simple and direct mechanism with a minimum of bureaucratic intervention.

Q 11. The preamble states that, "The BSCC is attempting to define what constitutes 'release into the environment'. The BSCC is establishing a working group on greenhouse containment and small field trials in order to develop scientific recommendations." When do you anticipate the task to be completed?

-- How are agencies defining containment and release in the interim?

A. The subcommittee on greenhouse containment and "release" is scheduled to report to the BSCC as a whole at the first meeting of the BSCC held in 1987. That report will be the first stage in a public process of developing these definitions and it is expected that the process will take until the middle of 1987.

At the present time the EPA has a functional definition of containment which can be found on page 23335 of the June 26, 1986 Federal Register notice. As I stated in the hearing, we view this definition as being very conservative and restrictive, however, it is functional and we feel confident that if we are erring, it is on the side of caution.

APPENDIX 2

PUBLIC AND SCIENTIFIC AFFAIRS BOARD
AMERICAN SOCIETY FOR MICROBIOLOGY

1913 I Street, N.W.
Washington, D.C. 20006
Telephone: (202) 822-9229

September 3, 1986

The Honorable James H. Scheuer
Chairman, House Subcommittee on Natural
Resources, Agriculture Research and
the Environment
U.S. House of Representatives
Washington, D.C. 20515

The Honorable Doug Walgren
Chairman, House Subcommittee on Science,
Research and Technology
U.S. House of Representatives
Washington, D.C. 20515

The Honorable Harold L. Volkmer
Chairman, House Subcommittee on
Investigations and Oversight
U.S. House of Representatives
Washington, D.C. 20515

Dear Congressmen:

The American Society for Microbiology (ASM) has developed the following responses, in the time permitted, to the three follow-up questions, which were posed in your letter of August 12, 1986, to the Society's July 23 testimony on federal regulation of biotechnology.

1. The original NIH/RAC guidelines for recombinant DNA research were overly cautious and conservative. They were relaxed as more information was obtained. Some critics suggest that the BSCC guidelines are "relaxed" before we have the environmental data to support that approach. How do you respond to this? We do not believe the Federal guidelines for regulating introduction of genetically altered organisms into the environment are overly relaxed as they presently stand. With the exception that we have already noted (organisms with foreign regulatory sequences), we believe the guidelines have identified all classes of novel organisms having potential for significant harm (assuming application of customary or reasonable protocols for their dissemination). Organisms with even a remote potential for harm are slated for scrutiny before use. Assuming that the "scrutiny" called for in the reporting mechanism used by one of the authorities (the Toxic Substances Control Act (TSCA)) entails evaluation and a potential for intervention if there are questions, then we are satisfied that all classes of organisms of interest will be examined before being put to new uses in the environment. We believe that many of these will be approved for use in the open environment and ultimately will be exempted from scrutiny. In other words, we think that the guidelines represent a cautious approach, casting a wide net, and we anticipate further relaxation in the future as more information is obtained.

2. Do the proposed federal guidelines have adequate provisions for the collection of information on genetically-engineered organisms? With respect to the mechanisms for collecting information on genetically engineered organisms, we think the avenues

blocked out in the guidelines for collecting pertinent information could be made to work, whether the avenue is a premanufacturing notice or an application for a use permit. Whether these mechanisms will in fact be adequate in practice depends on how the guidelines are interpreted and implemented in the form of specific information requirements and review practices.

Earlier we called attention to the fact that each case of planned release into an open environment will involve an interaction between a particular environment and a particular organism. It will be as important to collect information on the intended environment as on the organism. Permission to disseminate an organism should apply only to the type of environment that was evaluated for safety.

We believe that it will be possible to develop mechanisms for gathering pertinent information, although these details have not as yet been published.

3. For intrageneric organisms under TSCA, EPA is relying on Section 8(a) which requires companies to report certain data regarding production and use. Do you think such a reporting system to monitor these types of organisms is practical? Will a reporting requirement be a practical and effective instrument for monitoring particular classes of microorganisms under TSCA? The classes of microorganisms slated to be monitored by a reporting mechanism (as opposed to a full review) include genetically altered intrageneric nonpathogens and small scale (under 10 acres) trials of nonengineered pathogens. These categories of organisms do appear to be less risky than either intergeneric combinations or genetically engineered pathogens, thus the rationale for a lower level of review in these cases seems appropriate. How effective a reporting mechanism will be in monitoring uses of microorganisms will depend on the details of the form ~~the reporting~~ mechanism takes when new rules are promulgated.

We would favor an approach that would not view the reports under TSCA simply as instruments for gathering information, but as mechanisms for evaluation and validation of the experimental plans. We agree that the review process should be significantly shorter and simpler for the "report" categories compared to the categories specified for full review. So that the reporting mechanism could have a meaningful monitoring function, we favor placing a burden on the agency to review the reports within a reasonable period of time before the microorganism in question is scheduled to be applied to the environment so that any questionable case could be recommended for a full review before its scheduled introduction into the environment, but at the same time unnecessary delays would not interfere in cases that do not warrant further investigation.

We hope these responses will be helpful to the Members of the subcommittees and would be pleased to provide additional information.

Sincerely,

Jean E. Brenchley
Jean E. Brenchley, Ph.D.
President, American Society
for Microbiology

Harlyn O. Halvorson, Ph.D.
Chairman, Public and Scientific
Affairs Board, ASM

Monica Riley
Monica Riley, Ph.D.
Chairman, Committee
on Genetic and
Molecular Microbiology

APPENDIX 3

Environmental Law Institute
1616 P St. NW • Washington, DC 20036 • (202) 328-5150

September 10, 1986

Dr. Irene B. Glowinski
Science Consultant
Committee on Science and Technology
822 House Office Building Annex #1
Washington, DC 20515-6307

Dear Dr. Glowinski:

Enclosed are answers to questions posed in the August 12, 1986 letter to me from The House Committee on Science and Technology. These questions followed-up my testimony before the Subcommittee on Investigations and Oversight, The Subcommittee on Natural Resources, Agriculture Research and The Environment, and The Subcommittee on Science, Research and Technology on the federal regulation of biotechnology.

Question #1

The original NIH/RAC guidelines for recombinant DNA research were overly cautious and conservative. They were relaxed as more information was obtained. Some critics suggest that the BSCC guidelines are "relaxed" before we have the environmental data to support that approach. How do you respond to this?

1A. The BSCC definitions address an important and difficult issue — the scope of the authority the federal government intends to exercise in its regulation of engineered organisms. In essence, the BSCC definitions exempt certain categories of organisms from regulation. While it is reasonable and important to establish categories of organisms on the basis of the degree of hazard they represent, it is very early in the regulatory process to be exempting organisms from regulation.

A more sensible approach seems to be to err on the side of caution by including most engineered organisms within agencies' jurisdictions and then to enable and encourage the agencies to exempt categories of organisms from regulation on the basis of accumulated scientific information.

However, my major objection to the BSCC definitions is not that they are insufficiently cautious, but that they were arrived at without any public discussion of the critical scientific judgments they embody.

Question #2

Do the proposed federal guidelines have adequate provisions for collection of information on genetically-engineered organisms?

2A. Generally, no. Moreover, the guidelines contain no mechanism to systematically compile the information that will be collected by agencies so that it can be used in determining what are the actual risks associated with the releases of engineered organisms.

Question #3

For intrageneric organisms under TSCA, EPA is relying on Section 8(a) which requires companies to report certain data regarding production and use. Do you think such a reporting system to monitor these types of organisms is practical?

— EPA intends to promulgate "significant new use" rules that would require companies to report planned releases of intrageneric organisms that are pathogenic. Is this an appropriate and effective way to monitor the release of such organisms?

3A. a) If vigorously implemented, Section 8(a) is probably adequate for monitoring activities involving engineered organisms. But I believe it could prove an inadequate mechanism for responding to problem releases identified through the monitoring process. Problems might arise in the following situation. What if EPA receives 8(a) notice of an intrageneric organism about which it has concerns and would like to restrict the dissemination of the organism pending the development of more information. What recourse does the agency have? If the organism is not regulated under Section 5 of TSCA (PMN and SNUR), the only way to regulate organisms is under existing chemical or imminent hazard provisions of the statute. These provisions are procedurally so burdensome that the agency will find it impractical, except in egregious cases, to follow up on the leads the 8(a) notices provide.

b) Although "pathogenic" is an admittedly crude surrogate for "ecologically harmful," the approach is a satisfactory one for the time being.

Question #4

Under FIFRA, EPA has divided organisms into two classes. Level one — which includes intrageneric organisms, non-pathogenic organisms, and indigenous organisms — receives abbreviated review prior to small scale field testing. Do you agree with this approach?

4A. Generally, yes.

Dr. Irene B. Glowinski
September 10, 1986
Page Three

Question #5

The functions of Institutional Biosafety Committees (IBC'S) with respect to USDA funded biotechnology research are outlined on p. #23390 of the June 26, 1986 Federal Register notice.

- Is is your impression that the IBC will be the level at which the most rigorous oversight will be given to biotechnology based research proposals?
- Do you think that IBC's, as they are presently devised, will be capable of adequately carrying out these responsibilities?

5A. Probably not.

IBC's vary tremendously in their make-up, dedication and performance. It is hard to generalize about them, but it seems unlikely that local committees, however constituted, are the proper vehicle for implementing policy in an area as scientifically underdeveloped as this one. To begin with, IBC's cannot be counted on to have the requisite ecological expertise to answer, or even to ask, questions about ecological impacts. Furthermore, it seems unlikely that scientific reviews done by scattered local committees could ever generate the kind of information that would be useful in resolving the questions about scientific risk.

If you have any additional questions, please feel free to call.

Very truly yours,

Margaret G. Mellon
Director, Toxic Substances Program

Enclosure

APPENDIX 4

[illegible]
DAN GLICKMAN, Kansas
ROBERT A. YOUNG, Missouri
HAROLD L. VOLKMER, Missouri
BILL NELSON, Florida
STAN LUNDINE, New York
RALPH M. HALL, Texas
DAVE McCURDY, Oklahoma
NORMAN Y. MINETA, California
MICHAEL A. ANDREWS, Texas
TIM VALENTINE, North Carolina
HARRY M. REID, Nevada
ROBERT G. TORRICELLI, New Jersey
FREDERICK C. BOUCHER, Virginia
TERRY BRUCE, Illinois
RICHARD H. STALLINGS, Idaho
BART GORDON, Tennessee
JAMES A. TRAFICANT, JR., Ohio

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE AND TECHNOLOGY
SUITE 2321 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515
(202) 225-6371

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SID W. MORRISON, Washington
RON PACKARD, California
JAN MEYERS, Kansas
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
HARRIS W. FAWELL, Illinois
WILLIAM W. COBEY, JR., North Carolina
JOE BARTON, Texas
D. FRENCH SLAUGHTER, JR., Virginia
DAVID S. MONSON, Utah

HAROLD P. HANSON
Executive Director
ROBERT C. KETCHAM
General Counsel
JOYCE GROSS FREIWALD
Republican Staff Director

August 12, 1986

Dr. Elliott A. Norse
Ecological Society of America
730 11th St., NW, Suite 400
Washington, DC 20001-4584

Dear Dr. Norse:

Enclosed is a copy of the transcript from the July 23, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources, Agriculture Research and the Environment, and the Subcommittee on Science, Research and Technology on the federal regulation of biotechnology. Attached to the transcript are instructions for submitting requests for changes or clarification. Please review these instructions and the enclosed transcript of your remarks carefully. Your copy of the transcript, together with any written requests for changes, should be returned by September 3, 1986, to:

Dr. Irene B. Glowinski, Science Consultant
Committee on Science and Technology
822 House Office Building Annex #1
Washington, D.C. 20515-6307

The Subcommittees have developed some further questions as a result of the hearing. We would appreciate it if you would submit your responses to these questions when you return your transcript.

1. The original NIH/RAC guidelines for recombinant DNA research were overly cautious and conservative. They were relaxed as more information was obtained. Some critics suggest that the BSCC guidelines are "relaxed" before we have the environmental data to support that approach. How do you respond to this?

2. Do the proposed federal guidelines have adequate provisions for collection of information on genetically-engineered organisms?

3. Under TSCA, EPA has defined *inter*generic organisms as "new" substances subject to premanufacturing notification requirements, and all other organisms as "existing" organisms not subject to such requirements. Is this distinction workable and scientifically valid?

   -- Do you agree with EPA's policy under TSCA that *inter*generic organisms should be regulated through a notification system rather than a permit system?

4. For *intra*generic organisms under TSCA, EPA is relying on Section 8(a) which requires companies to report certain data regarding production and use. Do you think such a reporting system to monitor these types of organisms is practical?

   -- EPA intends to promulgate "significant new use" rules that would require companies to report planned releases of *intra*generic organisms that are pathogenic. Is this an appropriate and effective way to monitor the release of such organisms?

5. In a recent letter to *Science* magazine you wrote: "...The ability to develop new organisms has outstripped the ability to predict the consequences of their release. Research on these consequences and improved communications among researchers in all the relevant biological disciplines are essential before the public will accept the safety of biotechnology." Has the revised federal policy statement for the coordination of biotechnology policy addressed your concerns?

6. Is it your impression that the IBC will be the level at which the most rigorous oversight will be given to biotechnology based research proposals?

   -- Do you think that the IBC's, as they are presently devised, will be able to undertake the role of certifying that the research at a particular institution is in compliance with the guidelines of the various federal agencies?

Dr. Elliott A. Norse
August 12, 1986
Page 3

Your testimony at the hearing was extremely valuable to the Members, and we wish to extend our thanks for your participation and service to the Committee.

Sincerely,

Doug Walgren

James H. Scheuer
Member of Congress

Doug Walgren
Member of Congress

Harold L. Volkmer
Member of Congress

IG/lcg

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*Dr. Norse failed to respond to these questions. The hearing record officially closed on November 15, 1986 for written responses to the record.

APPENDIX 5

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 5 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Honorable James H. Scheuer
House of Representatives
Washington, D.C. 20515

Dear Mr. Scheuer:

In response to your letter of August 12, 1986 co-signed by Congressmen Walgren and Volkmer, I am enclosing two items. The first is the transcript from the July 23, 1986 hearing at which I testified on the regulation of biotechnology. My notes for clarification are indicated directly on the transcript. Second, I am enclosing responses to the seven questions that EPA was requested to answer.

Please let me know if I can be of further assistance.

Sincerely yours,

John A. Moore
Assistant Administrator
for Pesticides and
Toxic Substances

Enclosures

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Honorable James H. Scheuer
House of Representatives
Washington, D.C. 20515

Dear Mr. Scheuer:

In response to your letter of August 12, 1986 co-signed by Congressmen Walgren and Volkmer, I am enclosing two items. The first is the transcript from the July 23, 1986 hearing at which I testified on the regulation of biotechnology. My notes for clarification are indicated directly on the transcript. Second, I am enclosing responses to the seven questions that EPA was requested to answer.

Please let me know if I can be of further assistance.

Sincerely yours,

/s/ John A. Moore

John A. Moore
Assistant Administrator
for Pesticides and
Toxic Substances

Enclosures

RESPONSES TO QUESTIONS ON BIOTECHNOLOGY
from Congresspersons Scheuer, Walgren, and Volkmer
Letter of August 12, 1986 to Dr. John Moore

Question #1: The guidelines are not specific about the information a company would be required to submit to the Administrator under Section 8(a) of TSCA. How then does EPA plan to enable companies to voluntarily comply with the Section?

The Environmental Protection Agency (EPA) has not requested that companies voluntarily comply with the section 8(a) portion of its policy under the Toxic Substances Control Act (TSCA). The types of information that companies will be required to submit will be developed and established through the section 8(a) rulemaking process. The final rule will contain the necessary information to enable companies to comply.

In the EPA statement of policy on biotechnology, published in the FEDERAL REGISTER on June 26, 1986, EPA proposed a six-part strategy for microorganisms subject to TSCA. Each of the six parts is described in a separate unit of the FR notice. One of the six parts is now in effect: the requirement to submit a premanufacture notification (PMN) prior to manufacturing or importing "new" microorganisms. Another of the six parts of the policy, namely the section 8(e) requirement to report substantial risks, has been in effect since TSCA was enacted and EPA has simply reminded manufacturers, processors and distributors of their responsibilities under this part of TSCA.

EPA has requested voluntary compliance with two of the remaining four parts of its policy: reporting of "new" microorganisms prior to environmental release if release occurs as part of research and development, and reporting of significant new uses of pathogens and microorganisms containing genetic material from pathogens.

This leaves two aspects of the policy which are not currently in effect on either a mandatory or voluntary basis. One is the exemption from submitting a PMN for closed-system uses of new microorganisms. EPA is waiting for further information from public comments to determine whether such an exemption is feasible. The second is the section 8(a) reporting rule, which was the subject of your inquiry and is described above. Its purpose is to obtain information on all microorganisms subject to TSCA and released to the environment, but not otherwise reported.

Question #2: Under TSCA, small businesses are exempt from Section 8(a) reporting requirements. How and when will EPA address this problem with respect to genetically engineered organisms?

To address this problem, EPA believes that its current generic definition of "small manufacturer" in 40 CFR Part 704 may have to be modified in some way to reflect the size and financial situation of the average biotechnology business. Section 8(a) requires EPA to define "small manufacturer" by rulemaking. As EPA develops the section 8(a) rule for manufacturers and importers of microorganisms, the Agency will address the issue of revisions to the small manufacturer definition for the biotechnology industry. EPA is currently developing the 8(a) notice of proposed rulemaking, and expects to publish it in the Federal Register in Spring, 1987.

Question #3: How will EPA regulate the release into the environment of genetically engineered organisms from non-federally funded, non-commercial institutions?

Microorganisms used as microbial pesticides are subject to the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). Relevant requirements are specified in the June 26, 1986 Federal Register notice, and apply to all releases into the environment of genetically engineered (as well as other) pesticide products.

Microorganisms used for other purposes are generally subject to the Toxic Substances Control Act (TSCA). Section 5(i) of TSCA exempts non-commercial research and development from section 5 of TSCA. Therefore, non-commercial research with microorganisms is not subject to either premanufacture notification or significant new use notification requirements, as both of these are section 5 requirements.

Non-commercial research is not exempt from section 8 of TSCA, however. Thus EPA may require reporting of environmental releases involving non-commercial uses of microbes using the section 8(a) reporting requirement. This issue will be addressed during the course of the 8(a) rulemaking.

Question #4: Was Dr. Martin Alexander, a member of your scientific advisory committee, involved with the establishment of the guidelines and definitions? If so, please describe his involvement.

Dr. Alexander was involved with the establishment of the guidelines and definitions, inasmuch as he was one of many independent scientists whom we consulted on scientific issues underlying the policy. Specifically, he reviewed an early draft of the EPA policy and reviewed the proposed definitions at a specific point in their development.

In addition to Dr. Alexander, EPA consulted a number of independent scientists who are experts in the fields of microbial ecology, systems ecology, molecular biology, and related disciplines. Their comments are in the public docket. We would be happy to send copies of their comments if you would like to review them.

Question #5: EPA's policy statement allows manufacturers to publish in the Federal Register generic descriptions of microorganisms whose identity and/or use is claimed to be confidential business information. How can a generic description omitting identity and use give the public interested in submitting comments adequate notice of the nature of the organism being reviewed?

The requirement that EPA protect confidential business information is not unique to microbial products. Section 10 of FIFRA and section 14 of TSCA both prohibit EPA from releasing certain confidential business information, and the Agency must meet its obligation to protect information that is legitimately claimed as confidential. The Agency does have well-established procedures and mechanisms for reviewing CBI claims to ensure they are legitimate. We are encouraged by the extent to which submitters of microbial pesticides have been willing to release information. Also, as indicated in our June 26 policy statement, "the Agency also recognizes that there is a strong public interest in many aspects of biotechnology, particularly in the possibility of adverse effects resulting from the environmental release of genetically engineered organisms. Accordingly, it is the Agency's policy to carry out as much of its review as possible in the open, in order to provide an opportunity for public participation and to increase public confidence in the review process." The Agency has stated many times that it will strongly urge all submitters to permit the release and publication of sufficient information to allow the public to comment.

Question #6: At the hearing, Dr. Mellon testified that she felt the possibility existed under TSCA for an organism to be developed, go through the PMN process, go on the inventory with little or no review. At that point, according to Dr. Mellon, there would be no legal recourse available to those wishing to challenge the release of the organism. Please comment on this.

We would like to address this question in two parts. First, Dr. Mellon expressed the concern that a product could go through the PMN process and on to the Inventory with little or no review. The procedures that EPA has established and which are explained in detail in the June 26 statement of policy ensure that reviews will be extremely thorough and scientifically credible. The procedure includes detailed review by EPA scientists with assistance from independent scientists, and peer review by the Biotechnology Science Advisory Committee.

Under TSCA, once a microorganism is listed on the Inventory of Existing Chemicals, other manufacturers can use it without submitting a new PMN. This is true for chemicals as well as microorganisms.

The fact that a microorganism is on the Inventory means that it is not subject to PMN requirements, but it does not exempt it from other requirements of TSCA. In particular, sections 4, 6, 7, 8, and 13 of TSCA provide authority to regulate existing microorganisms under conditions that are specified in the statute. For example, section 6 allows the Administrator to regulate microorganisms if they may create a substantial hazard, and section 8 allows the Administrator to require reporting or record-keeping on existing microorganisms. Thus, these authorities provide EPA with legal recourse if there is reason to believe that a microorganism already listed on the Inventory could cause harm to human health or the environment. In addition, concerned citizens may petition EPA under TSCA section 21 to take certain regulatory actions.

Question #7: Dr. Morse testified at the hearing that the decision to focus on pathogens and organisms having intergeneric combinations suggests a serious misunderstanding of taxonomy and ecology. Additionally, he stated that the inter-generic criterion reflects inadequate understanding of variations among species in a genus, and that these differences could be crucial. Please comment on this.

EPA believes that its decision to give the closest regulatory scrutiny to environmental releases, pathogens, and organisms having inter-generic combinations represents a reasonable attempt to select those activities, from among a very large number of activities in the biotechnology industry, that deserve the most review and oversight at the federal level. The Agency's decision is based on extensive consideration of the current state of science. EPA consulted persons who are experts in the fields of microbiology, molecular biology, ecology, and taxonomy. These experts came from within the federal government, from the academic sector, and from industry. Some of these experts are members of the society for which Dr. Norse was testifying -- the Ecological Society of America. These scientists' comments suggested that there is a wide range of opinion among scientists as to the nature, magnitude, and likelihood of risks that may occur with genetically engineered (and other) microorganisms. Most of the scientists indicated that EPA's choice to focus particular attention on pathogens and inter-generic microorganisms is a reasonable way of integrating the uncertain and rapidly developing science with the statutory requirements. It was recognized that under both FIFRA and TSCA, the Agency will in any case review information on all other genetically engineered organisms prior to their release to the environment. This is felt to provide a reasonable safety net. In addition, EPA has striven to ensure that the policy gives it the flexibility to incorporate new scientific information as it becomes available.

STATEMENT OF JOHN A. MOORE, ASSISTANT ADMINISTRATOR FOR PESTICIDES AND TOXIC SUBSTANCES, U.S. ENVIRONMENTAL PROTECTION AGENCY

Mr. MOORE. Mr. Chairman, I would like to just highlight a couple of points that are in my testimony.

As the committee well knows, in December 1984 EPA proposed an approach to the regulation of biotechnology products under two statutes that it administers, the Toxic Substances Control Act as well as the Federal Insecticide, Fungicide, and Rodenticide Act.

EPA received comments from 71 organizations and individuals addressing a broad range of scientific policy issues after promulgation of that statement.

The elements--I am sorry--the comments proved to be extremely valuable to EPA in developing its current policy and, in fact, led EPA to revise its original proposal in certain significant respects. EPA's current policy, as described in the June 26, 1986, Federal Register notice, is based on public comments, discussions with many scientists, and experience in reviewing genetically altered microbial products during the year or year and three months that intervened between the two notices.

Probably the most significant change is that EPA has established different levels of review for different types of microbial products. In its 1984 proposal, it proposed to subject all genetically engineered microorganisms to the same level of regulatory scrutiny.

Based on comments that had been received, and further reflection on that point, we have tried to develop and have promulgated a system that basically tries to tailor the level of review to the nature of the change that was effected using biotechnology, and the degree of risk that may possibly be associated with the use of that material.

The agency's conclusion is that there are primarily three categories of microorganisms that currently deserve the closest regulatory attention. These three types that we will most closely review under both FIFRA and TSCA are: microorganisms with new characteristics or that are new to the environment in which they are ~~[illegible]~~ proposed to be used; microorganisms that have hazardous components in them, either they are ~~were~~ pathogenic or receive genetic material ~~something~~ from a pathogenic organism; or, thirdly microorganisms that are used in the environment--and parenthetically, they therefore have the potential for widespread exposure.

Now, to translate that general approach into the Toxic Substances Control Act, we basically are talking about microorganisms that would be altered through deliberate human intervention to contain genetic material from dissimilar source organisms. They would be considered new, which is a critical component for being captured under TSCA.

Therefore, [illegible] ~~it~~ would be subject to premanufacture notification requirements.

EPA, and the other regulatory agencies as well, define the word ''dissimilar'' as organisms from different taxonomic genera. The organisms resulting from such a combination then would be called ''intergeneric.''

Now, in order to implement this, we basically are going to have to get into four rule promulgations. Very briefly--which are also described in my written statement--we are going to have to get into a rule that allows PMN review during the early stages by making a modification to the current research and development exemption.

Secondly, we're going to write a significant-new-use rule that will basically allow us to confront and review [illegible] ~~altered~~ genetic material that ha~~ve~~s come from the pathogenic organism sources.

Thirdly, at the lower level of review, we're going to promulgate a rule under section 8(a), which basically is a requirement that people will notify EPA in advance of any proposed field experiments.

Then, lastly, we are also entertaining the possibility that we might exempt certain types of organisms under section 5(h)(4) of the Toxic Substances Control Act. Whether we do that and how we do that will be strongly contingent on the nature of the comments that we have asked to receive in our June 26th notice. Since we haven't received those comments yet, we certainly can't draw judgments as to how, if, and under what set of circumstances we would do such.

EPA's current policy under FIFRA modifies the scope of what was the interim policy by providing again for ~~[illegible]~~ these two levels of notification and review. The three categories of microorganisms that would deserve the closest degree of scrutiny ~~is~~ are similar to that which I have just described that would be appropriate to both TSCA and FIFRA.

We shouldn't lose sight of the fact that it has always been the case that FIFRA's experimental-use-permit provisions must be observed for all pesticides, regardless of whether or how they were manipulated, prior to field tests involving anything greater than one acre of water or ten acres ~~in~~ of land.

Again, the level and type of review that we will give are the same under EPA's current policy as ~~well do it was~~ they were under the interim policy. In essence, we have solicited and have been successful, I believe, in getting scientists who possess expertise appropriate to the specific issue to partake of their time to give us the benefit of their expert opinion as well as the opinion of agency scientists during the evaluation of these pesticides. This has been done on an ad hoc basis under the aegis of the Scientific Advisory Panel which is mandated under FIFRA. I think that process has worked well. We intend to continue to use that process ~~whether in the throes of~~ as we promulgat~~ing~~e a biotechnology sciences advisory board on behalf of the whole agency -- so that function probably will transfer from the scientific advisory panel on an ad hoc basis ~~under~~ to this new committee that is in the process of being formed.

EPA feels that its policy ensures that those biotechnology products that currently deserve close scrutiny will be properly reviewed. I might parenthetically say that they are being properly reviewed, given that we have looked at nine submissions in the last year under the pesticide program, and that future changes to the regulatory program can be adopted, and that clear guidance is available to this young, but important and vulnerable industry.

The agency believes that its policy will help the public to understand that the products of genetic engineering encompass many possibilities, many of which that--are of modest or minimal concern. Therefore, the products' characteristics should determine the appropriate level of scrutiny in this case by the Federal Government.

That concludes my statement, Mr. Chairman.

[Statement of Mr. Moore follows:]

********** INSERT **********

Mr. VOLKMER. Thank you very much, Dr. Moore.

Dr. Bentley?

Mr. VOLKMER. Thank you very much, Ms. Darling.

I would like to start with a few questions here for Dr. Moore.

Under TSCA, if an organism is altered by just the deletion of genetic sequences, such that it exhibits new traits, why wouldn't it be considered a ''new'' organism?

Mr. MOORE. It would not be ~~could~~ considered new but it could ~~and would~~ be reviewed under TSCA. We certainly would review it and probably put it under an extensive review if the organism that you started with in making the deletion was one that came out of a ~~genus or a~~ species that was held to be pathogenic.

Mr. VOLKMER. But if it was nonpathogenic?

Mr. MOORE. Once ~~If it was is anything that~~ what we are ~~were~~ proposing to do with these rules is in place, if it was nonpathogenic, it would still be subject to our 8(a) notification rule prior to any experiment, but it would not be subject to the intensive review.

Mr. VOLKMER. Who makes the decision as to what is pathogenic, and how do they make that decision?

Mr. MOORE. Congressman, ~~in a number of instances,~~ classic reference texts are available to define~~, I think~~, for the vast majority of circumstances what is pathogenic and what is not. In those instances where the potential regulated individual may have doubt as to whether or not they should be covered or are not covered, our statement strongly encourages that they consult with the agency and maybe prudence would dictate in ~~that~~ those circumstances they presume it's pathogenic, if in doubt, until we tell them it's not.

Mr. VOLKMER. Well, because I can envision that you could have an intrageneric transfer between a host that is nonpathogenic but has traits towards pathogenicity and the same type of genera that is pathogenic being placed within that host and could possibly end up with a pathogen, could you not?

Mr. MOORE. Yes. I think the way something like that could happen is that if indeed you had something that was at low level in a ''nonpathogenic'' organism and indeed you manipulated its genome such that it starts to express that in far greater quantity, it might then find itself in the circumstances that it now becomes some type of a concern.

We would hope that indeed, since you have to notify us under section 8 prior to going forward, that we would have the opportunity to catch that.

Mr. VOLKMER. What if they didn't?

Mr. MOORE. Well, if the regulation was in place and they didn't, I guess they would go on with their experiment until we caught them. But I would say if they ignored our regulation, they would probably go along until we caught them as well. Then once caught and if indeed found to have done something wrong, if the regulation was in place--

Mr. VOLKMER. If you found it to be pathogenic, then it's in violation of the regulation. Now, prior to the promulgation of our significant-new-use rule, and that is going to be probably, what, nine, ten months, maybe a year before we have that in place?

Mr. MOORE. Typical.

Mr. VOLKMER. How do you learn of releases into the environment of existing organisms?

Mr. MOORE. Congressman, as we sit here today, with the exception of an individual who may be at the stage of feeling that they want to commence commercial manufacture of an organism, anything that they must do that might fall under the purview of TSCA has to be done on a voluntary basis.

Mr. VOLKMER. And if they don't do it, there is no violation?

Mr. MOORE. Correct.

Mr. VOLKMER. Now, you correct me if I am wrong, but presently under TSCA substances used for research and development, not for commercial, are exempt from premanufacturing notification and significant-new-use reporting. Is that correct?

Mr. MOORE. That's correct.

Mr. VOLKMER. How are you planning to address this problem?

Mr. MOORE. That is one of the rulemakings that we are

For purposes of clarification please substitute the following for lines 3396 to 3402. As they now read, these lines (which were misstated) are very confusing.

3396 Mr. Moore: That is true. Under both FIFRA and TSCA, we have stated in our policy that indigenous, non-engineered pathogens do not have to be reported until they will be released on 10 acres or more of land. Under FIFRA, this policy has been in place since the interim policy was issued in November 1984. Under TSCA, EPA has requested voluntary compliance with this policy towards pathogens until it issues a significant new use rule. During the rulemaking process, the issue of whether indigenous, non-engineered pathogens should be included in the scope of the rule will be raised for public comment. In the meantime, EPA has requested voluntary compliance and has advised persons that for purposes of voluntary compliance they should report indigenous, non-engineered pathogens prior to release on 10 acres or more--the same policy as we have under FIFRA. 3402 working on to make organisms subject to reporting and not ~~to~~ under the R&D exemption that currently exists.

Mr. VOLKMER. Do you have sufficient statutory authority to do that?

Mr. MOORE. We're reasonably comfortable that TSCA can get into that.

Mr. VOLKMER. All right. What about under TSCA, the testing on fewer than 10 acres without prior review by EPA?

Mr. MOORE. Now, there is no reference to either 10 acres of land or one acre of water under TSCA. That's an existing regulation of FIFRA which was for general application to all pesticides. We basically are saying, under TSCA, that you should consult with us too--at a minimum--through a notification--and in those instances that we have concerns as it relates to, say, the more extensive organisms, you must report to us.

Mr. VOLKMER. I am looking at the Federal Register, June 26, and it says indigenous pathogens, prior notification and review, none if it's under 10 acres.

Mr. MOORE. Under TSCA?

Mr. VOLKMER. Under TSCA.

Mr. MOORE. That would be true because the reference of ~~either acres~~--either 10 acres or one acre, depending on land or water, is something that is unique to FIFRA in regulation, and there is no ~~reference~~ regulation as it relates to TSCA.

There is no regulation in place that speaks to size limitations ~~as to whether~~ such that if you're under it, you don't have to report.

Not correct. See attached language for correction.

Mr. VOLKMER. So you would say they would have to report?

Mr. MOORE. Yes. I would say that under TSCA, ~~as far as~~ if you had to report, you would ~~not~~ have a cutoff as a function of size of your planned experiments, for some types of pathogenic micro-organisms.

Mr. VOLKMER. All right. Now, the guidelines divide genetically engineered organisms into two categories for review under FIFRA. Why was this done, and what is its effect?

Mr. MOORE. Basically, one thing that I try to impress upon both the Office of Toxic Substances and the Office of Pesticide Programs, we are promulgating a policy that, given that we were talking about biotechnology in organisms, ~~that~~ I wanted consistency between the two policies unless there was a very convincing reason as to why it should not be consistent. The result of that ~~would be what as we~~ as finally promulgated in our June notice, compared to what was our interim policy under FIFRA, we basically went from ~~what was~~ report everything or at least consult with EPA's pesticide program on everything, to a program of consult on everything or at least notify on everything. But indeed we implemented this two-tier review, depending upon the nature of the concern.

I think the practical outcome of the two-tiered review as it relates to pesticides is probably more apparent than it is going to be real, because the nature of the organism or the nature of what you are working with and what you propose to do is going to suggest that it causes deleterious effects or else you wouldn't be looking at it as a potential pesticide. So it probably would be captured anyway.

Mr. VOLKMER. Now that we have our new guidelines in place and you're developing your new rule, assuming that those rules would be in place and the guidelines, as we know, are subject to review, but let's say they're all in place and for the first time AGS comes in and says we're developing this ice-minus stuff with gene deletion on a bacteria existing, nonpathogenic. You're going to treat them differently than you treated them in the fall and spring of this year?

Mr. MOORE. If somebody came in with ice-minus and it was similar, if not identical, to either the AGS or the Lyndow~~e~~ request, which was in the genus Pseudomonas, ~~we would~~ they would be subject to the intensive review of the two-part review that we're talking about.

If they came in with a proposed ice-minus type of an experiment which was in a nonpathogenic species, they would get the lower-tier review.

Mr. VOLKMER. So it depends upon the pathogenicity of the product?

Mr. MOORE. Yes.

Mr. VOLKMER. All right. Now, noncommercial R&D is exempt by law, is that correct, not regulation, under TSCA?

Mr. MOORE. Noncommercial would be exempt under section 5, yes.

Mr. VOLKMER. What about--

Mr. MOORE. If a company--

Mr. VOLKMER. That's a minor change in the law?

Mr. MOORE. Right. Congressman, a company that is not deriving any funds from a Federal source ~~and therefore be imposed by the NIH guidelines or USDA guidelines or something like that,~~ as it sits right now, if they were totally non commercial and it was nonpesticidal in nature, they would be exempt.

Mr. VOLKMER. After reviewing what is--and the problems with developing guidelines and regulations under TSCA, for any possible biotechnological chemical products, should TSCA be changed to a permitting scheme like FIFRA?

Mr. MOORE. People have raised this previously and said wouldn't it be simple to have a prospective and a positive scheme whereby before you could move forward--akin to FIFRA. In some respects, it would have some intuitive appeal. On the other hand, I think if you did it under TSCA, you would be significantly changing TSCA from the way it was perceived, at least the agency perceives, as to what was intended when it was permitted--when it was enacted.

FIFRA, for example, there's no question, FIFRA is a licensing statute and that is not the intent of TSCA. TSCA is a listing statute and a review mechanism. So it would be a very significant change.

I think that we do have a reasonable chance of being able to adequately control the biotechnology industry under the existing statutes of TSCA. As to whether or not one will be able to do it with the ease and facility that we all might like, I think it's probably best to answer when we get a little bit of experience. We have yet, as we sit here, to receive the first thing under TSCA.

Mr. VOLKMER. Right. I think we all understand that. But on the other hand, I think some of us again that are laymen, in looking at this, realize that TSCA was developed for a chemical industry which is a lot different from a biotechnology industry where you're going to have possible microbial bacteriological uses that have different traits than chemicals. That's what I think concerns some of us.

Now, OSTP recently commissioned a report on risk assessment methods for biotechnology. It stated in the report that important requirement in the risk assessment process is detailed knowledge of the environmental and pathogenic characteristics of the modified microorganisms.

Now, will the premanufacturing notice of 8(a) reporting requirements address this?

Mr. MOORE. We would hope so. We may have to go about it indirectly. Let me take a minute to explain what I mean by that. TSCA is written to not require data upfront to be in the same envelope as the request for consideration to be added to the inventory.

I think what the agency plans to do is to identify the types of information it thinks is required in order to make an informed judgment. ~~if~~ I indeed the regulated industry doesn't listen to what that is, or fails to heed what I think ~~is~~ are reasonable recommendations, we would then be in a position that we should receive something absent such data. I think that we would be required under section 5 to basically sit there and say that, hey, we think we have a presumption here of may present possible risk or widespread exposure, which is in the statute, and either hold up the granting of the study, or put it under tight requirements by a section 5(e) consent order or something like that. That would probably have the net effect of forcing them to go back and generate the data.

Mr. VOLKMER. You're going to be able to do that, to show that, without the data?

Mr. MOORE. We think we can do that much easier with a living microbe than we can with the chemical because of the statement in the statute that speaks to wide exposure. By the very nature of a living organism going out into the environment, I think that's a priori evident that there is potential for wide exposure.

Mr. VOLKMER. Now, if EPA allows the release of an intergeneric pathogen, let's say, on one acre of land in Florida or anyplace else, the organism goes on the inventory and anyone can release it anywhere unless EPA adopts a significant-new-use rule that requires notification before using it again elsewhere, like 400 acres in my district in Missouri, and 10,000 acres in Kansas. Is that correct?

Mr. MOORE. Yes. Unless we made some type of restriction at the time we allowed something to go on the inventory, once it is on the inventory, it is totally unrestricted. Our intent would be, I think, early on, to work under a presumption that indeed we likely will put it under a 5(e) order ~~where the person who was requesting the PMN and either put it under a--~~ or make it subject to SN~~E~~UR to make sure other people can't do things we're preventing the original requester to do, or something similar to that, some type of a restricted inventory category where you cannot do what you are hypothesizing.

Mr. VOLKMER. All right. Now, have you--and I believe you touched this somewhat, and I know Dr. Bentley and Ms. Darling touch this on their end--have you appointed any contact people to work with the USDA on applications where there would be overlapping jurisdictions?

Mr. MOORE. Yes, sir.

Mr. VOLKMER. Those have been appointed?

Mr. MOORE. Yes. We have in every instance--I believe, in every instance--that we've had the nine organisms that have been requested, we have had communication with USDA and indeed have had participation on the part of USDA in their comments as to the appropriateness of what concerns they may have. Even if they didn't have a statutory handle, we want their advice at any rate, and in some instances ~~there~~ it is quite appropriate that while we might be having the lead to review the organism in this case, they would point out that, hey, a license--I am sorry--a permit may be required, particularly under the Plant Pest Act.

Mr. VOLKMER. Let's assume that USDA reviews it and they make recommendations that further tests along a certain area, a certain review be done, and your EPA scientists don't agree with that. Now what happens?

Mr. MOORE. All right. Well, I think I can put it in--just generally speaking--

Mr. VOLKMER. Or is that just not going to happen?

Mr. MOORE. Oh, I think it will happen, if it hasn't already happened. I think it will happen, scientists being what they are.

Mr. VOLKMER. They might have some disagreement?

Mr. MOORE. Indeed, there may be disagreement or there may be something that scientist A thought about that scientist B didn't think about, or scientist B thought about and didn't think it was that big a problem, so failed to mention it.

I think when you get a circumstance like that, whether it be EPA, USDA, or whether it's just two scientists in general, we want to sit down and ~~see if~~--get the two to start to communicate with each other to see why they seem to have a different perspective.

In my experiences, in most instances, the vast majority of circumstances, they both moderate and ~~s~~come to something that is more common to both of them. That is not to say that that happens in all instances. If you end up in an instance~~--in some instances~~ where ~~there~~ some scientist says, hey, I understand everything you're trying to tell me but I still think that I might be right, then I guess that's where I get paid for my money for making [illegible] a decision as to what do you do in that circumstance.

Mr. VOLKMER. Does a Level I review under FIFRA and the TSCA report requirements require less data than Level II and PMNs?

Mr. MOORE. Let me make sure I understood your question. A Level II review, under either statute, probably would end up having much more data being evaluated than would a Level I.

~~That is~~. It is entirely conceivable, however, that the first piece of correspondence that the agency received could contain the same amount of data and then after we said, wait a minute now, this is going to require more intensive review, we would then ask for additional and then receive ~~that more~~ additional data. If I understood your question right.

Mr. VOLKMER. All right. Now, is--correct me if noncoding regulatory sequence changes are in the lower level of review.

Mr. MOORE. Yes, they would be.

Mr. VOLKMER. Can you tell me why they are?

Mr. MOORE. Well, within the definition, we talk about the exclusion of ~~possibly~~ regulatory sequences, ~~in this case, being now~~ based on the ~~judgment of~~ scientific judgment that indeed these types of sequences don't pose any major problems.

Mr. VOLKMER. Now we will start on the other side. We'll start on USDA for a while. Now I was just given a copy of the July 21, 1986, briefing books this morning, Dr. Bentley, of your memorandum, along with Mr. Tracy, in regard to the issuance of license, permits, or approvals of agricultural biotechnology permits. Is that everything that's supposed to be forwarded to the director of the office of agricultural biotechnology? Correct?

APPENDIX 6

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

September 10, 1986

Honorable Harold L. Volkmer
Chairman, Investigations and Oversight Subcommittee
on Science and Technology
U.S. House of Representatives
2321 Rayburn House Office Building
Washington, D.C. 20515

Dear Mr. Chairman:

This replies to your letter of August 12, 1986 following up on our testimony of July 23, 1986 on the research and regulatory aspects of agricultural biotechnology. Your letter included several additional questions on biotechnology research and regulation and our responses to these questions follow.

1. Question: To whom in USDA will the proposals for release of genetically engineered organisms go?

1.1 Who will review them?

Answer: Under the proposed USDA Guidelines for Biotechnology Research, release proposals that are funded in whole or in part by USDA will be submitted to the USDA Office of Agricultural Biotechnology (OAB) through the local Institutional Biosafety Committee (IBC). OAB will prepare the proposal for the Agricultural Biotechnology and Recombinant DNA Advisory Committee (ABRAC). The ABRAC, following the NIH-RAC model will review and provide a recommendation to the Assistant Secretary for Science and Education who will then announce approval or other disposition of the proposal. Proposals not funded by USDA may be submitted to the OAB on a voluntary basis.

USDA's Animal and Plant Health Inspection Service (APHIS) has the authority to regulate genetically engineered organisms pursuant to the authority granted by the Virus-Serum-Toxin Act (VSTA), the Federal Plant Pest Act (FPPA), and the Plant Quarantine Act (PQA).

Proposals for field trials of recombinant-derived veterinary biologics (defined at 9 CFR 101.2(w)) are sent to and reviewed by APHIS' Veterinary Services (VS).

USDA has proposed to establish regulations under the authority of the FPPA and PQA for the introduction (importation, interstate movement, or release into the environment) of genetically engineered organisms or products which are plant pests or which there is reason to believe are plant pests (regulated articles) at 51 FR 23352-23366 on June 26, 1986. Under the provisions of this proposed rule, a permit from APHIS' Plant Protection and Quarantine (PPQ) would be required prior to the movement of a regulated article into or through the United States or interstate, or release into the environment. Such permit applications would be sent to and reviewed by PPQ.

USDA under the FPPA and PQA, and the Environmental Protection Agency (EPA) under the Toxic Substances Control Act (TSCA), jointly review genetically engineered microorganisms intended for nonagricultural use, but which may be pathogenic to plants. The chart and text published at 51 FR 23358-59 on June 26, 1986, explain the conditions for USDA-EPA joint review. Chart I published at 51 FR 23304 on June 26, 1986, lists the reviewing agencies' jurisdiction for various genetically engineered products.

1.2 Will both the Science and Education and Marketing and Inspection Division have input into reviews of release proposals?

Answer: Yes. USDA's Office of Agricultural Biotechnology (OAB) under the purview of the Assistant Secretary for Science and Education, receives notification of the receipt of and action on all recombinant applications submitted to APHIS. This notification procedure (see attached) provides the means for communication between S/E and M/I on such submissions and actions. The OAB will notify APHIS of proposals submitted through OAB.

Biotechnology release proposals that are funded in whole or in part by USDA will be submitted to the OAB through the local Institutional Biosafety Committee (IBC). OAB will review each research proposals and determine if it should be reviewed and discussed by the Agricultural Biotechnology and Recombinant DNA Advisory Committee (ABRAC).

2. Question: Will any division or group outside APHIS review applications to license or move a genetically engineered product?

Answer: The establishment of the Office of Agricultural Biotechnology (OAB) and the Intra-Departmental Committee on Biotechnology in Agriculture (CBA) are administrative mechanisms to assist in determining those instances in which wider review of proposed releases would be appropriate and beneficial.

In general, divisions and/or groups outside APHIS review applications to license or move a genetically engineered product as follows:

(1) APHIS's VS uses the "Interagency Group to Monitor Vaccine Development, Production, and Usage" to consider potential human health hazards from the use of veterinary biological products and to review such issues as the potential effects of organisms that may be pathogenic to humans or animals.

(2) Biotechnology committees in both VS and PPQ will review recombinant applications for licensing (VS) and release into the environment (PPQ) of recombinant-derived organisms. These committees will include scientists from outside APHIS.

(3) The procedure described in APHIS' August 8, 1986 memorandum for notification to the OAB provides a formal mechanism for transferring information to the OAB about all recombinant applications received by APHIS. In general,

APHIS notifies the OAB 5 working days after receiving a license or permit application, and 10 working days before final action on such an application. The OAB may request additional information about an APHIS action on a licensing or permit application.

Additional review may be accomplished on an "as needed" basis using mechanisms both within and outside of the Department consistent with Federal laws, rules, and regulations.

2.1 In the past, officials of APHIS have said that only APHIS personnel may review applications containing confidential business information. Now we hear that the OAB and the ABRAC will review certain applications. Is this a new interpretation of existing policy or has the agency policy been altered?

Answer: Employees of the Federal Government, including special Government employees may not divulge confidential business information. Members, consultants, and advisors associated with both ABRAC and NBIAP, neither of which entities have existed in the past, will be "special Government employees." As such, they will be authorized to review confidential information after they have signed a commitment to protect such information. In such reviews, the reviewers will be required to act consistently with the Trade Secrets Act (18 U.S.C. 1905).

3. Question: Will proposals to release genetically engineered organisms at Federally-funded institutions be reviewed and approved at the local IBC level?

Answer: The Advanced Notice of the USDA Guidelines of June 26, 1986 (51 FR 23367) states that research experiments involving release of genetically engineered organisms not exempt from the Guidelines require IBC and USDA approval before initiation. In addition, research proposals for release of genetically engineered organisms not covered by an exemption or a safety precedent will be reviewed at the national level by the OAB and by the ABRAC.

3.1 If a researcher disagrees with an IBC decision, can the researcher appeal to the agency?

Answer: Although it is not explicit in the advanced notice, it is intended that if researchers disagree with an IBC decision, they are free, as in the NIH/IBC system, to appeal to the national level. In that case, OAB would then determine whether to concur with the IBC, reverse the IBC, or refer the question to ABRAC.

3.2 Is the agency considering altering the present policy regarding membership of the IBC?

Answer: The IBC's were included as an element of the NIH/RAC procedure. The USDA proposes to use these same committees to avoid duplication of effort. The membership of specific IBC's may need some supplementation to assure capability to evaluate agriculture-related proposals and to comply with the membership requirement in the proposed USDA Guidelines (Section 403, 51 FR 23389). The Department expects to be working closely with NIH on this matter in the near future.

3.3 Who will monitor the IBC's?

Answer: Overall responsibility will continue to rest with NIH. In agricultural matters, however, the OAB will monitor the composition and decisions of each IBC for compliance with the USDA Guidelines. In addition, ABRAC will have the responsibility under the USDA Guidelines to assure the IBC's agriculture-related capability and will cooperate with NBIAP at the local level.

3.4 Can the agency legally delegate the majority of its oversight in this area to the IBC's? If so, is such a delegation practical?

Answer: The Food Security Act of 1985 (P.L. 99-198) authorizes the Secretary of Agriculture to establish appropriate controls over the application of biotechnology to agriculture. The controls envisioned in the advance notice of the proposed USDA Guidelines are, in our judgment, measured and appropriate. We stress that the Department has not proposed to delegate Federal government approval when such approval is appropriate. Nor has it proposed to delegate its oversight responsibility. These responsibilities are the Department's to exercise, but it intends to build on the experience of the NIH-RAC system.

3.5 Will proposals from commercial institutions be reviewed and approved at the local IBC level?

Answer: Although the proposed Guidelines do not require compliance by commercial institutions, USDA expects that they will comply voluntarily. To encourage compliance, the Department anticipates offering non-Federally funded researchers the opportunity to have their proposals reviewed. Proposals from commercial entities may be reviewed at the local level if they have an IBC. OAB will assist firms in identifying possible IBC's with which to work. Many commercial firms will have significant incentives arising from insurance needs, public relations, and subsequent requests for regulatory approval to submit proposals voluntarily to OAB/ABRAC for review. Again, the precedent for this mode of operation has been set by the NIH/RAC/IBC system whereby commercial institutions have voluntarily established an IBC to oversee recombinant DNA laboratory research or large-scale production.

4. Question: Will a commercial institution applying to APHIS for a product license have to verify that all applicable research guidelines were followed in order to obtain a license?

Answer: In order to receive a veterinary product license, a firm must also have an establishment license issued by APHIS. USDA requires that commercial institutions applying for a product license verify that all applicable regulatory standards and guidelines be followed in product development. Licenses for the production of veterinary biological products are only issued under the Virus-Serum-Toxin Act (21 U.S.C. 151 et seq., 9 CFR Part 102).

4.1 Will the IBC have to certify the conditions under which the experiments were performed?

Answer: APHIS will require IBC or equivalent review and approval of the research program prior to the initiation of any project employing recombinant DNA technology. IBC's certify that the proposed research program has been correctly categorized and that they are in compliance with the appropriate guidelines.

4.2 Under the Virus-Serum-Toxin Act, at what point in a product's development can USDA exercise its regulatory authority?

Answer: All aspects of research and development programs carried out in a USDA licensed establishment are subject to regulation by APHIS under the Virus-Serum-Toxin Act (VSTA). It should be noted that the 1985 amendments (December 23, 1985, P.L. 99-198, Title XVII, Section 1768, 99 Stat. 1654, 1655) expanded the jurisdiction of the Virus-Serum-Toxin Act to include intrastate commerce and exportation.

5. Question: Assume that you have two companies involved in developing a product eligible for licensing under the VSTA. The first company performs an unauthorized field test with the product. The second company then obtains the product from the first company and applies for a VSTA license based on the data from the unauthorized field test. Will USDA allow the second company to support the product based on data from the unauthorized field test?

Answer: Data from an "unauthorized field test" performed by Company A cannot be used to support a USDA license application by Company B.

An applicant for product license must demonstrate that all tests necessary to show that the product is safe, pure, potent, and efficacious. One of the initial steps in the licensing process is the preparation, characterization, and APHIS' acceptance of Master Seed stock (virus or bacterial culture).

Once the Master Seed is certified for use in a product, this material is used to prepare pre-licensing serials of vaccine as well as all vaccine that will be used to determine safety and efficacy data. Because this information must be developed by the license applicant, the data from unauthorized field trials is essentially unusable in the APHIS licensing procedure.

6. Question: Who within USDA will be responsible for preparing an environmental assessment or impact statement prior to releasing or licensing of genetically engineered organisms?

Answer: The agency responsible for taking action on the submission for a license, permit, or approval of a biotechnology report is responsible for compliance with the provisions of the National Environmental Policy Act (NEPA) (42 U.S.C. 4321 et seq.) and the regulations published by the Council on Environmental Quality (CEQ) at 40 CFR Parts 1500-1508. USDA has determined that NEPA is best implemented by reliance on USDA agency procedural guidelines. For example, the "APHIS Guidelines Concerning Implementation of NEPA Procedures," were published at 44 FR 50381-83 on August 28, 1979. The APHIS Guidelines set forth the procedures that APHIS' PPQ and VS use to prepare an environmental assessment or an environmental impact statement prior to the release or licensing of a genetically engineered organism. APHIS is in the process of revising its guidelines to implement changes in CEQ's regulations, to take into account recent scientific developments and APHIS' experience to deal with evaluation of the environmental effects of its programs. When NEPA guidelines are adopted for agricultural research proposals involving release of genetically engineered organisms, OAB will be able to determine the need for environmental assessments and oversee their preparation using information supplied by the principal investigator.

7. Question: The Science Committee recently released a GAO report stating that USDA was funding 87 research projects that could lead to environmental release of genetically engineered organisms within the next five years. Has USDA made the investigators of these research projects aware of the procedures they must follow in order to get approval for an environmental release?

Answer: Principal investigators or their administrators are advised of both current and proposed procedures for review and approval of environmental releases. The proposed procedures are currently open to public comment.

7.1 Have any of these proposals been submitted to USDA for approval yet? If yes, to whom? If not, when do you expect to start seeing them?

Answer: We have not yet received any proposals for environmental release from these investigators. We anticipate such submittals following the comment periods, final decision and implementation of procedures.

7.2 Has the Department made copies of these 87 research proposals available to other Federal agencies which might have jurisdiction over the products to be released?

Answer: When the proposals are received and our final procedures are implemented, project information will be provided to agencies which might be involved with product release for commercialization.

7.3 How is the Department going to be able to develop the information it needs to review applications if it fails to fund any risk assessment research?

Answer: The Department funds both risk assessment and impact assessment research. The risk assessment aspects are now part of most protocols and will be growing as the number of research projects increases. Specifically, they will be incorporated into the research project protocols. Similarly, impact assessments will be developed in research projects under the National Biological Impact Assessment Program (NBIAP) to track biological changes over time and most especially as the mass of a given biotic component is increased in nature through agricultural practices.

8. Question: Has the ABRAC been officially established? If so, please provide us all documents relating to its establishment, functions, and makeup?

Answer: The Department's proposal to establish ABRAC has been announced, but its charter will not be formally approved until the conclusion of the comment period. In the interim, the Agriculture Recombinant DNA Research Committee will continue to fulfill the functions ascribed to ABRAC. Its proposed functions are described in 51 FR 23391 published on June 26, 1986.

8.1 Will the ABRAC have the authority to review confidential business information?

Answer: The ABRAC will be provided with any information needed to discharge properly the responsibility assigned to it by the Department, which may include confidential business information. USDA will assure that ABRAC members act consistently with the provisions of the Trade Secrets Act (18 U.S.C. 1905).

9. Question: How will USDA regulate genetically engineered products that may not necessarily be plant pests, but could still be detrimental to society?

Answer: Concerns about issues that may be "detrimental to society" frequently surface in the research stage during review by the Institutional Biosafety Committees and if an environmental release is involved, the proposal is submitted to outside scientific review through a RAC-like process. Thus, this process will often occur prior to development of a product, i.e., in the research stage.

With respect to product development and marketing, USDA does not have the statutory authority to regulate products specifically designated as "detrimental to society." Without further definition of the term "detrimental to society," regulatory jurisdiction cannot be assigned. The intended use of the product must also be identified before jurisdiction can be determined. If such a product were intended for use as a pesticide, it would be regulated by EPA under the Federal Insecticide, Fungicide and Rodenticide Act, as amended. If the product were a food, food additive, or drug, it would be regulated by the Food and Drug Administration (FDA); if a controlled substance, it would be regulated by the Treasury Department. The statutory definition of plant pest in the FPPA is broad enough to include genetically engineered products that pose a threat to agriculture, and, in this sense, could be considered "detrimental to society."

9.1 Can USDA require pre-release review under the (Federal) Plant Pest Act?

Answer: Under the provisions of the proposed USDA rule pursuant to the FPPA and PQA, APHIS will require a permit prior to the introduction, which includes release into the environment, of a genetically engineered organism which is a plant pest or which USDA has reason to believe is a plant pest. Proposed Section 340.0(a) prohibits any person from introducing a regulated article unless the introduction is authorized by a permit and such introduction is in conformance with all of the applicable restrictions contained in Part 340 (51 FR 23353, June 26, 1986).

9.2 How will USDA regulate a genetically engineered product when its plant pest status is unknown?

Answer: Under USDA's proposed rule pursuant to the FPPA and PQA, USDA will, in effect, regulate genetically engineered organisms whose plant pest status is unknown. Genetic engineering techniques permit the combination of genetic material that would occur infrequently in nature. The resulting traits may be new to the organism or the environment into which it is released. Such genetically engineered organisms may exhibit new or altered traits affecting survivability, host range, or competition. USDA will regulate genetically engineered organisms or products when one or more of its constituents--donor, vector, vector agent, or recipient--comes from a family or genus of organisms known to contain plant pests. USDA believes that such an organism must be regulated because certain undesirable traits may be transferred to the new organism and may survive when the organism is released into the environment.

Under the provisions of USDA's proposed rule, a person wishing to introduce a genetically engineered organism would consult Section 340.2, "Groups of organisms which are or contain plant pests." USDA has not attempted to list every pest species in this section, in part because the pest status of many species is unknown. Proposed Section 340.2 lists higher taxa which include known pest species. In addition, USDA has reason to believe that groups of organisms which are currently unclassified or unknown are likely to contain plant pests and, therefore, are included in proposed Section 340.2. USDA has specifically requested comments on proposed Section 340.2 (See also Federal Register announcement of June 26, 1986.)

9.3 Has USDA ever regulated any product of unknown plant pest status?

Answer: USDA regularly evaluates plants and plant products whose plant pest status must be determined. To evaluate the plant pest potential of such an organism, an extensive investigation is undertaken, which includes surveys of acknowledged scientific specialists and international, national, State, and local officials and a search of the scientific literature.

10. Question: Is the Department of Agriculture required to provide a public comment period when it reviews applications to release genetically engineered organisms? If not, does the Department plan to do so voluntarily?

Answer: Applications for approval of research proposals involving release of genetically engineered organisms will be reviewed by ABRAC. The ABRAC meetings will be open to the public to the extent permitted by the Trade Secrets Act and agendas will be announced in the Federal Register. This procedure will allow the public an opportunity for comment.

In reviewing applications for the release of genetically engineered organisms into the environment, USDA is guided by the procedures set forth in the NEPA. For example, APHIS has determined that prior to the issuance of permits for release of such organisms, an environmental assessment will be prepared. Appendix I of the "APHIS Guidelines Concerning Implementation of NEPA Procedures," published at 44 FR 51273 on August 31, 1979, provides for publication in the Federal Register of the results of such an environmental assessment and a finding of no significant impact. Furthermore, if the environmental assessment finds that an environmental impact statement is in fact necessary, a notice of intent to prepare a statement will be published in the Federal Register.

If we can supply any further information on these or other questions, please let us know.

Sincerely,

Orville G Bentley
ORVILLE G. BENTLEY
Assistant Secretary
Science and Education

Karen Darling
KAREN DARLING
Acting Assistant Secretary
Marketing and Inspection Services

Attachment

United States
Department of
Agriculture

Animal and
Plant Health
Inspection Service

Washington, DC
20250

August 8, 1986

Subject: APHIS Procedure for Notification to OAB
Genetically Engineered Organisms

To: Orville G. Bentley
Assistant Secretary
Science and Education

This memorandum outlines the procedures to be used by the Animal and Plant Health Inspection Service (APHIS) in notifying the Office of Agricultural Biotechnology (OAB) of the receipt of and action on submissions for licenses, permits or approvals of agricultural biotechnology products. Notification to the OAB about these submissions is in response to Mr. Tracy's and your memorandum on this subject dated July 21, 1986.

All notification to the OAB by APHIS will be made by the Biotechnology and Environmental Coordination Staff (BECS). The two APHIS agencies concerned with biotechnology, Veterinary Services (VS) and Plant Protection and Quarantine (PPQ), have developed the procedures described below for reporting information to the BECS, which will in turn transmit the information to the OAB. In general, BECS will notify the OAB 5 working days after receiving a license or permit application, and 10 working days before final action on such an application. Exceptions are noted below.

A. VETERINARY SERVICES

Under the authority granted by the Virus-Serum-Toxin Act of 1913 (21 U.S.C. 151-158), the U.S. Department of Agriculture (USDA) exercises regulatory authority over all veterinary biologics imported into the United States or shipped or delivered for shipment interstate, intrastate, or exported. Veterinary biological products must be prepared in a USDA-licensed establishment, and products imported into the United States must be imported under a permit.

BECS will report on the licensing of veterinary biologics derived by recombinant techniques as follows:

Category 1 - inactivated recombinant DNA derived vaccines, bacterins, bacterin-toxoids, virus subunits and bacterial subunits, monoclonal antibody products used prophylactically, therapeutically, or as components of diagnostic kits:--provide to OAB lists of products licensed, updated monthly. Since these products are inactivated, they do not present a risk of release into the environment, APHIS' notification on these products is different from those products in category 2 and 3.

Category 2-3 - live genetically engineered organisms having simple gene additions or deletions or that include the use of live microorganisms as vectors:

- License applications - notification to OAB of receipt within 5 working days.

- Authorization (permit issuance) of field trials—notification to OAB 10 working days prior to transmitting a decision to the applicant.

- License issuance - notification to OAB 10 working days prior to transmitting a decision to applicant.

(VS proposes to devise a form to use as the transmittal vehicle to provide notification of license application, approaching licensing action, and decision on issuance.)

BECS will report on the permitting of imported veterinary biological products as follows:

- Permits for genetically engineered live veterinary biological products for research and evaluation under conditions of containment or for transit shipment provide to OAB lists of permits issued, updated monthly. Since these permits do not involve release into the environment and usually granted within a short time period, notification for these permits is different than those permits which involve release into the environment.

- Permits for genetically engineered live veterinary biological products for research and evaluation that involve conduct of field trials: notification to AOB 10 working days prior to transmitting a decision to applicant.

- Permits for distribution and sale of genetically engineered live veterinary biological products: notification to OAB 10 working days prior to transmitting a decision to applicant.

- Permits issued for importation or transport of organisms and vectors for research under conditions of containment: list updated monthly for (a) live animal pathogens that have been modified by the addition or deletion of one or more genes; (b) live microorganisms (non-pathogens) that have been modified to carry recombinant-derived genes obtained from animal pathogens; (c) genetic material derived from animal pathogens intended to be incorporated into live microorganisms by genetic engineering techniques.

B. PLANT PROTECTION AND QUARANTINE (PPQ)

Pursuant to the authority granted by the Federal Plant Pest Act (FPPA) of 1957, as amended (7 U.S.C. 150aa-jj), and the Plant Quarantine Act of 1912, as amended (7 U.S.C. 151-154, 166-167), USDA has regulatory authority over the movement into or through the United States, or interstate, of plants, plant products, plant pests and any product or article which may contain a plant pest at the time of movement. The FPPA and PQA are applicable to the plants, plant products and other articles and plant pests developed through genetic engineering if such plants, plant products, other articles or plant pests present a risk of of dissemination into the United States or interstate of plant pest introduction, spread, or establishment.

APHIS' PPQ will report field trial and permit submissions for genetically engineered organisms as follows:

- Field Trial
  - notification within 5 working days of receipt of the request.
  - notification of action 10 working days before a decision is transmitted to the applicant.
- Permit
  - importation and interstate movement under containment for laboratory use.
  - notification within 5 working days of receipt of application; notification of action 10 working days prior to transmitting a decision to the applicant.

Submissions listed by accession number by PPQ and product code by VS contain trade secret and confidential commercial information, and are processed in conformance with the APHIS requirements for the control and protection of confidential business information (CBI) published at 50 FR 38561-63 on September 23, 1985. Trade secret and confidential business information are exempt from disclosure under section (b) (4) of the Freedom of Information Act (5 U.S.C. 552(b)(4)), and thus any request for additional information about the submissions accorded accession numbers or product codes should be made in conformance with section VIII of the APHIS CBI requirements.

The reporting format for APHIS submissions which contain CBI will include the accession number or product code and an abstract describing the process or product. All communication from the OAB about notification procedures and the subject APHIS submissions shall be conducted through the BECS.

Bert W. Hawkins

Bert W. Hawkins
Administrator

DEPARTMENT OF AGRICULTURE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20250

September 9, 1986

Dr. Irene B. Glowinski
Science Consultant
Committee on Science and Technology
House of Representatives
822 House Office Building Annex #1
Washington, DC 20515-6307

Dear Dr. Glowinski:

Enclosed is a copy of the corrected transcript from the July 23, 1986, hearing before the Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources, Agriculture Research and the Environment, and the Subcommittee on Science, Research and Technology on the regulation of biotechnology.

We are also enclosing two items which we hope can be included in the record. The first is a memorandum concerning submissions that contain confidential business information; the second is the publication: "Veterinary Biological Products: Licensees and Permittees*/ which includes an appendix listing licensed biotechnology products.

If we can be of further assistance, please let us know.

Sincerely,

Karen Darling

Karen K. Darling
Deputy Assistant Secretary
Marketing and Inspection Services

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*Not included in printed hearing transcript. This publication can be obtained from the Animal and Plant Health Inspection Service; published July 1986.

Enclosures

Washington, DC 20250

Notification of Submissions--
Genetically Engineered Organisms

John Patrick Jordan
Administrator
Cooperative State Research Service

JUL 21 1986

Pursuant to the authority granted by the Federal Plant Pest Act, as amended (7 U.S.C. 150aa-150jj), Plant Protection and Quarantine (PPQ), Animal and Plant Health Inspection Service (APHIS), has received the following submissions (referenced by accession number):

I. Referrals from the Environmental Protection Agency:

000029
000001
000027
000002
000022
000028
000032
000033

II. Referral from Science and Education: Calgene submission

III. Submitted directly to APHIS:

000019
000021
000018
000026
000024
000025
000030
000033

The submissions listed by accession number contain trade secret and confidential commercial information and are being processed in conformance with the APHIS requirements for the control and protection of confidential business information (CBI) published at 50 FR 38561-63 on September 23, 1985. Trade secret and confidential business information is exempt from disclosure under section (b)(4) of the Freedom of Information Act (5 U.S.C. 522(b)(4)), and thus any request for additional information about the submissions accorded accession numbers should be made in conformance with section VIII of the APHIS CBI requirements.

This memorandum constitutes notification of the receipt by APHIS of the above-referenced submissions. It is in fulfillment of the reciprocity agreement through which APHIS will receive corresponding notification from Science and Education of all research submission received by your office.

/s/ Bert W. Hawkins

Bert W. Hawkins
Administrator

Copies to [illegible] / Wood / Kelley
Dailey / [illegible]

cc:
O. Bentley, Science and Education, Washington, DC

APHIS:OA:SIngebritsen:slt:436-8896:07/21/86:SI0703-86:BT#7/11

BIOTECH-LICENSED PRODUCTS

Category I-A: Bacterins

	PRODUCT	CODE NO.	LICENSED FIRM	ESTAB. NO.	DATE LICENSED
1.	E. Coli Bacterin for Swine	26R8.56	Norden Laboratories	189	July 16, 1984
2.	E. Coli Bacterin for Swine	2648.08	Salsbury Laboratories	195	October 5, 1983
3.	E. Coli Bacterin-Toxoid for Swine	7850.00	Norden Laboratories	189	March 15, 1983
4.	E. Coli Bacterin-Toxoid for Swine	7900.RO	Norden Laboratories	189	June 29, 1984
5.	E. Coli Bacterin for Swine	26R8.44	Salsbury Laboratories, Inc.	195	December 23, 1982

Category I-B-1: Therapeutic or Prophylactic Use

	PRODUCT	CODE NO.	LICENSED FIRM	ESTAB. NO.	DATE LICENSED
1.	E. Coli Monoclonal Antibody for Newborn Cattle	3525.00	Molecular Genetics Inc.	284	November 8, 1983

Category I-B-2: Used in Diagnostic Kits

PRODUCT	CODE NO.	LICENSED FIRM	ESTAB. NO.	DATE LICENSED
1. Feline Leukemia Virus Test Kit	5028.00	Pitman-Moore Inc.	264	August 22, 1979 *October 7, 1982
2. Equine Infectious Anemia Antigen and Reagent Serum	5515.20	TechAmerica Diagnostics	272-A	June 28, 1984
3. E. Coli K99 Antigen Test Kit	5032.00	Molecular Genetics Inc.	284	January 29, 1985
Feline Infectious Peritonitis Antibody Test Kit	5029.00	TechAmerica Diagnostics	272-A	November 21, 1984
Feline Leukemia Virus Antigen Test Kit	5028.00	Biologics Corporation	317	October 30, 1985
Pseudorabies Virus Antibody Test Kit	5110.01	AgriTech Systems, Inc.	313	January 16, 1986
Pseudorabies Virus Antibody Test Kit	5110.02	AgriTech Systems, Inc.	313	January 16, 1986
Feline Leukemia Virus Test Kit	5028.00	AgriTech Systems, Inc.	313	June 6, 1986
Equine Infectious Anemia Antibody Test Kit	5514.00	TechAmerica Diagnostics	272-A	June 13, 1986
Equine Infectious Anemia (For Further Manufacture)	E514.00	Syngene Products and Research, Inc.	272-B	June 13, 1986

New Biotech component added

Category II: Live Gene Deleted

	PRODUCT	CODE NO.	LICENSED FIRM	ESTAB. NO.	DATE LICENSED
1.	Pseudorabies Virus Vaccine Modified Live Virus	1891.RO	Biologics Corporation	272	January 16, 1986

STATEMENT OF KAREN DARLING

Ms. DARLING. Thank you, Mr.Volkmer. It's been a long day. I have learned something. I hope we all have.

I don't want to take much time to talk about some of the regulatory authorities and functions of the Department of Agriculture except for the Animal and Plant Health Inspection Service, because there ~~have~~ has certainly been some comment about how we operate ~~at~~ APHIS today. I will go into a little bit of background on how APHIS is represented in the biotech policy statement and how we've stated that it's our perspective that we can regulate new or novel products in the same manner that we have Regulated traditional products because of a variety of statutory authorit~~y~~ies. ~~as so granted.~~

I think it important to keep in mind as well that in this broad authority ~~that we have~~ under the Plant Pest Act, the Virus Serum Toxin Act, the Plant Quarantine Act and so forth, that we also have our emergency statutes that let us quarantine or stop movement thereof or, as we do so well, kill animals or kill plant pests or other actions ~~the exercise~~ that we take to put down a danger to the society.

Certainly, we are not people ~~with~~ at the Department of Agriculture or throughout the Government that want to release something into the environment that might be dangerous. ~~And~~ Speaking as a regulator and someone also worried about budgets, I don't want to have to spend so much money to put down whatever it is that might cause the problem.

We regulate the veterinary biological products, animals and poultry, plant and plant products, meat and poultry products, seeds and other articles under~~, and there are~~ a variety of statutes. Those have been enumerated in the Federal Register from the first Federal Register notice in December '84.

Under the authority granted by the Virus Serum Toxin Act, the USDA regulates veterinary biological products produced in the United States or imported into the U.S. The Food Security Act of '85 amended the Virus Serum Toxin Act by expanding USDA's authority over such products in several respects. Under the amended statute, it is unlawful to ship or deliver for shipment any worthless, contaminated, dangerous, or harmful biological product intended for use in the treatment of animals anywhere in or from the United States. Previously, intrastate shipments and exports were not subject to that act.

It is also unlawful, subject to certain exemptions, to ship biological products unless they were prepared in compliance with regulations prescribed by the Secretary of Agriculture in an establishment licensed by the Secretary.

The 1985 amendment also extends the Secretary's rulemaking authority and contains new enforcement provisions.

It is taking a bit of time to get everything, every proposal set forward under the Virus Serum Toxin Act because of changing all the regs, all the rules, to reflect both intra and interstate movement as well as import-export.

Currently, we have about 70 establishment licenses out there and about 1,400 product licenses for veterinary biological products. In the context of a biological product, certainly we are concerned about any biological product, whether it be derived from genetic engineer~~ed~~ing or a traditional method. We're talking about a live virus; we're talking about moving it.

And we do not permit any movement of any biological product without a permit from the USDA. So we have what I feel is ~~a~~ good control all the way through the chain. You cannot go from the laboratory to the field without having a permit from the USDA.

Products which are imported into the United States must also be imported under permit issued by the Secretary,and we've issued about a thousand permits under the Virus Serum Toxin Act to perform that function.

Veterinary biological products derived by recombinant DNA techniques or ~~that are~~ developed from hybridomas are categorized o~~therwise are listed~~ in the '86 notice. ~~We have-- we feel that~~ Each product is evaluated individually to determine what will be necessary to establish its purity, safety, potentcy and efficacy. Scientific considerations may dictate generic areas of concern or ~~for~~ require the use of certain tests under specific situations. Special assays, preferably using in vitro methods, may be required for potency and stability determinations. Additional tests may be required to assure safety, especially when live microorganisms are present in the biological product.

The rest of the statement I believe you have before you, and I would like to request that it be submitted into the record. I feel that Dr. Bentley has spelled out very well the coordination that we now have in place and which has been written down and signed off by the Secretary of Agriculture as to the function of the office of Agricultural Biotechnology ~~which will~~ assure the coordination as well as the inherent cooperation~~--but will ensure the coordination~~ within the Department of Agriculture both from the research arm and the regulatory arm.

The coordination that we have with ~~out~~ other regulatory agencies, like the Environmental Protection Agency~~,~~ and the Food and Drug Administration, ~~have~~ has also developed into certain processes by which we deal with each other. With the Environmental Protection Agency we correspond back and forth. We ask one another to have an overview of a particular product application that may be in the pipeline, to assure that all the regulatory agencies involved in that particular product feel that we have an efficacious product.

I think we've come a long way since we began this process in April '84. It has certainly been a study in human dynamics as well as looking at the science of this very important process.

I think we've had a pretty long day and I shouldn't say too much more except to say we welcome your questions.

[Statement of Ms. Darling follows:]

********** INSERT **********

Mr. VOLKMER. How does OAB react with ABRAC?

Mr. BENTLEY. Well, ABRAC would be--it would react in this way; that is, when materials--let us say now that a proposal came in for a research proposal that had release into the environment and was clearly one that needed to--that should be reviewed or at least be given consideration under the guidelines, it would be the one that--it would be the office to get the material to the appropriate chair of the ABRAC to get the process under way. That would be one reaction.

The other reaction might be, in ABRAC, if there was a question that came up in the regulatory--if there was such a question--it could help facilitate getting the material to the ABRAC committee in an expeditious way.

Mr. VOLKMER. Again going back to the serum or the vaccine, and I am a commercial firm and all my research has been done in house without any agency funding, and I have done my laboratory research and now I want to test it out, and I have got a facility owned by my organization. Let's say I am going to use cattle, something for bruc~~i~~ellosis; I am going to get rid of bruc~~i~~ellosis with this new serum. So I go out and we start shooting, and it turns out, hey, this thing is working. A year later, after I find out that it's working, I sell it off to XYZ corporation over there, and now XYZ is going to--they file an application for a license with APHIS.

Now, can XYZ use that test results in support of the license?

Ms. DARLING. Mr. Chairman, in support of a license or any application for permit, all data that has been collected or is being collected should ~~would be advisable to~~ be submitted at that time. As you know, in APHIS we have all kinds of scientists. They're not necessarily all research scientists, but we've got all kinds of scientists that, while they are notifying the OAB that your XYZ has come in with an ~~their~~ application based on your herd, ~~that~~ our staff reviewer--

Mr. VOLKMER. This is the ''Volkmer corporation'' that did it all, but I have sold it over to XYZ.

Ms. DARLING. I hope they got a pretty penny for it.

Mr. VOLKMER. Pardon?

Ms. DARLING. I hope you got a pretty penny for it and decided to patent it.

Mr. VOLKMER. Oh, yes, we've got a lot of money now. But you--

Ms. DARLING. We've been looking for--

Mr. VOLKMER. You never have heard about this before. We didn't let you know we were doing it.

Ms. DARLING. Until you wanted to move it inter or intrastate--

Mr. VOLKMER. No, I didn't tell you that.

Ms. DARLING. Well, you didn't tell us--

Mr. VOLKMER. I never did tell you.

Ms. DARLING. But you're going to now because you want to commercially--

Mr. VOLKMER. No, I am not. XYZ is. I am not.

Ms. DARLING. Because you're selling to XYZ.

Mr. VOLKMER. I sold everything. I sold all manufacturing rights and all the information, how to make it and everything else, the process and everything, to XYZ.

Ms. DARLING. So XYZ is coming to APHIS to say--

Mr. VOLKMER. Right.

Ms. DARLING.--hey, have we got a product here we want you to look at.

Mr. VOLKMER. Right.

Ms. DARLING. And I would--probably I am being a little presumptive, but I would presume that all data that has been collected to that point would certainly be admissible to be looked at.

Now, at the same time, we are extremely concerned with the confidential business information to not let out that XYZ really was Volkmer and company's development.

Mr. VOLKMER. Well, that doesn't make any difference. My point--I am trying to get at a point I think you're missing, Ms. Darling, and that is that all the testing was done under the new guidelines, et cetera, as I understand it, and I transported this serum even intrastate interstate, as I understand it, is supposed to be illegal. I've done all that illegally and you're going to let XYZ use all that information, though. That's what concerns me.

Ms. DARLING. When they submit their application?

Mr. VOLKMER. They submit their application to you and the only test results they show are the ones that we ran and you didn't even know we were doing it.

Ms. DARLING. I see what you're getting at now.

Mr. VOLKMER. Yes.

Ms. DARLING. Yes, because we cannot--we cannot restrict research or statutorily say this is how you have to run that test before you bring it to us.

Mr. VOLKMER. Right. Now, you can restrict the flow of serum if you find out that, supposing under your new rules you are going to be able to restrict the flow of serum both intra and interstate, but you got to remember my facilities are in a little town and my herd is right outside of town and nobody is going to even know about it. And I didn't even know I was supposed to do it.

[Laughter]

Mr. VOLKMER. You know, I'm a young guy, a little guy, and I didn't even know I was supposed to do that. See, that's one of the things I want to point out that I--

Ms. DARLING. Yes, I understand.

7

Mr. VOLKMER.--think concerns me.

Dr. Bentley, would that concern you, that you're able to use that even though--that information--even though it was illegally done?

Mr. BENTLEY. Yes, it would.

Mr. VOLKMER. And you can't stop it, though?

Ms. DARLING. No.

Mr. VOLKMER. So that's something I think you better look at.

Now, I have submitted that to--XYZ has submitted it to APHIS. When XYZ submitted that data and the application for the license, et cetera, all to APHIS, APHIS sent a notice over to OAB. Correct?

Ms. DARLING. Correct.

Mr. VOLKMER. Now, OAB has got this notice and looking at it and saying, ''Hey, that's just another--that's a bruc~~i~~ellosis vaccine or eradication serum; that's fine stuff. It doesn't look so bad to us.'' What will happen as far as the ABRAC is concerned? Will they get into it?

Mr. BENTLEY. This, of course, is plowing some interesting ground. But let me say this, that if this came to the--as it comes to the OAB and as I would envision it--one could ask if it is a genetically modified organism and that's what was used to produce the bruc~~i~~ellosis--and I presume that's your--

Mr. VOLKMER. Right.

Ms. DARLING. Well, Mr. Chairman, you know, I certainly understand their concern. Yes, we regulate plant pests. We are charged with regulating plant pests. Beneficial pests aren't necessarily something that come into an emergency situation ~~by~~ which APHIS needs to regulate ~~beneficial pests~~. But certainly, we are charged with protecting the American food and fiber system ~~to try to~~ we work with ~~like~~ EPA, to hold down the plant pest population.

I think she is totally wrong in her assessment of how that is viewed, but she will have her opportunity to talk to the Plant Pest Act on the 29th of January in Sacramento, or the 5th of August in this town.

Mr. VOLKMER. The 29th of July?

Ms. DARLING. 29th of--yes--July, to make her comments and thoughts public, to go into the record on the amendments or proposed amendments to the Plant Pest Regulations ~~Act~~.

Mr. VOLKMER. But, in other words, as I understood her point, you can have genetically engineered organisms, products, that could be not necessarily plant pests, but could still be detrimental to society in general. What about those?

Mr. BENTLEY. Could I speak on that?

Mr. VOLKMER. What about that type of--

Mr. BENTLEY. There are two points. The guidelines, as I understand and interpret it, says that all organisms--that is, genetically modified organisms--are subject to review before release, prepared release into the environment. And we spoke on the TSCA and on FIFRA discussions, and that would apply. And the same thing, therefore, I think that all organisms would be covered in some way in the guidelines, so as far as the organisms are concerned, microorganisms.

Mr. VOLKMER. All right.

Mr. BENTLEY. Now, with regard to research that would be covered, I didn't read this from my testimony, but in the testimony I point out that the USDA guidelines would encompass all phases of agricultural biotechnology research, and we're talking here of contained laboratory experiments, specialized isolation research, as in greenhouses and biotrons, environmental research releases, whether uncontrolled or segregated field plots.

All of these are types of things that would be controlled and would be subject to review if they fell under the guidelines, so that we would--and I guess the best way I can describe it is by analogy, would be that many of the kinds of proposals that have gone to the NIH RAC that relate to agricultural crops or agricultural uses of products would come to Agriculture.

We will handle them in much the same way that has been done over the past few years.

Mr. VOLKMER. That will be part of the OAB?

Mr. BENTLEY. Yes. It would be--the OAB provides us not only as a functional office but a staff person that can devote time to being sure that these kinds of arrangements can be made, communications person, just to facilitate who makes the call, who makes the contact.

Ms. DARLING. And aside from that, we already have two parent committees in APHIS that are in contact with ~~over contact with~~ EPA.

Mr. VOLKMER. All right. You have had some already contact with them, like on the Monsanto application.

Ms. DARLING. We certainly did.

Mr. VOLKMER. And you made recommendations and it appears that those have pretty well worked out between EPA and USDA?

Ms. DARLING. In that case, EPA had requested the USDA to review that application, which we ~~so~~ did. The EPA asked for a second of our own opinion, and we also tendered that, and it was their decision it was a product that was clearly within th~~ose~~e jurisdiction~~s~~ of the EPA. But appropriately, as set out in the policy framework, they ~~have~~ asked us for our review. We will, in turn, do the same thing on anything that looks like a cross-jurisdiction. Of course, we do have those.

Mr. VOLKMER. Okay.

Does the gentleman from California have any questions?

Mr. PACKARD. Thank you, Mr. Chairman.

I have four questions. May I just request for the record--repeatedly the witnesses have indicated a flow--even to the extent of perhaps a flowchart of one authority and one agency to another and within the agencies, one function or of one committee to another. I think it would be helpful if the committee could actually get, if it's available, the flowchart of the review process.

Mr. BENTLEY. Yes.

Mr. PACKARD. What you have, I think we ought to have in terms of--because several questions have been in relation to how the different committees will review and from there where it goes. Any comment?

Mr. BENTLEY. Mr. Packard, we have such a sheet. We have it laid out, a chart. We've taken pictures of it and so on. We would like to just, if I may, we would be glad to submit that to the committee. We would like to review it once more. We made a lot of changes and a lot of things in the last ten days or so that we would like to look at. But we have a chart for you.

[Information to be furnished follows:]

********** COMMITTEE INSERT **********

Mr. PACKARD. Thank you. Under the Noxious Weed Act, would you be kind enough to explain how the statute can be used to require prerelease review of genetically engineered plants? Doesn't the regulation of such a weed require a rule and public notice and public hearings, examples of weeds regulated under the act clearly show that a plant has had to spread considerably before the rule could be promulgated? I was wondering if you could explain how that proceeds.

Ms. DARLING. Mr. Packard, I understand we're not utilizing the Noxious Weed Act in the context of the proposals of the policy statement, but more under the Plant Quarantine Act and the Plant Pest Act rather than the Noxious Weed Act.

Mr. PACKARD. So the procedure then, would it be changed under the new guidelines?

Ms. DARLING. From the Noxious Weed Act?

Mr. PACKARD. Yes.

Ms. DARLING. Not that I envision.

Mr. PACKARD. Okay. Also, we have not discussed, to my knowledge, penalties. Again, I apologize for not being able to be here during the full hearing. The penalties for violation, I would be interested in knowing how penalties will be applied, whether they will be applied to institutions or researchers, individuals, or both, and whether they will be consistent with the penalties of other agencies and so forth. Would you wish to respond?

Mr. BENTLEY. I think that is really at least two major parts to the answer to that. Let me treat the one that has to do with research. The one, for an agency that does not comply with these rules, let's say, a university that's getting funding from--part of all of its funding for a project from USDA, we can withhold funding of program--withhold the allocation of funds. That is the major hammer that you do have, and this can be, having been in the university most of my career, I know that that can be applied and it can be applied in times when it becomes rather critical. We hold up the release of funding. You usually hope you never come to that that kind of a situation, but that would be, in the final analysis, one of the ways.

Now, there are other penalties, specific penalties that have to do with license and permits which I don't--I am not familiar with, and so I would turn to Karen.

Ms. DARLING. Actually, in ~~breaking~~ violating a statute under the APHIS~~, under the APHIS statutes~~, we have civil penalties, criminal penalties, and administrative penalties. Administrative action, we could withdraw a permit if a permit had been activated; ~~W~~we have civil fines, and ~~Y~~you can always turn it over to the Justice Department for a criminal investigation.

Mr. PACKARD. Are they--are most of the penalties planned o considered directed at the institution, or does the researcher themselves become involved in penalties?

Ms. DARLING. I would envision whoever makes that application.

Mr. BENTLEY. In a case of research, I think since most of the funds are institutional, it would be to the institution; that is, if a State agricultural experiment station has a fund of money that comes to that institution. In a case of individuals, I am not positive of that, but the mechanisms that I have ever been familiar with, it went via the institution to the investigator.

There haven't been too many of those, but that's the way it's been applied, because when the private investigator--''private investigator,'' I didn't mean that--the research investigator develops a proposal, it has to have--through the university system, it has to have some institutional commitment or else it wouldn't be a proposal. That would only handle it. So the institution is the one you have to get back to in that case.

Now, an individual disobeying of the law, of some law that pertains thereto, such as fraud or other kinds of statements, then it goes to the individual.

Mr. PACKARD. So an individual, if an individual is actually in violation at one institution, that individual would not be able to move to another institution and still continue the funding on a project? It's not--it couldn't transfer the funds?

Mr. BENTLEY. No. There have been some wonderfully creative people that have done some things like that in their life, and I am always amazed at it when they can do it. But normally, that would not be the case. So I am--because there is too much institutional communication and agency communications to do this.

We would hope that the violation part would be on the minor side, that we would be mostly dealing with that, and I am sure that's the way you mean it, too.

Mr. PACKARD. Yes.

Ms. DARLING. Mr. Packard, my counsel ~~just~~ advises that submitting a false application could be a felony crime.

Mr. PACKARD. I see. How do your regulations apply to laboratory work that is not conducted by institutions, done by private firms, perhaps even without Federal funding?

Mr. BENTLEY. Well, the guidelines say that it does not necessarily directly apply to people that are funding their own research or carried on in the private sector. However, if that moves to--that involves a plant pest, for example, that that does. Those guidelines apply. It doesn't make any difference whether it's public or private. Or if they go to release a genetically modified material into the environment on a planned way, on a controlled way, that applies.

For conducting research on a modified product in a laboratory, it is not a requirement but we have the feeling that many people would like to work on a voluntary basis. That's work that has been very effective in the NIH situation where people sought the additional confirmation and additional confidence in their own decisions on the way they handle their products, they sought as much advice and help as they could. I think that from our conversations that we've had with some of the major biotech firms large and small, that they are going to be seeking the same thing in the case of the USDA.

Mr. PACKARD. How would you normally be aware of experimentation being done by a small private firm that has not done business through your agency before? How would you know that they were doing any research?

Ms. DARLING. We don't.

Mr. PACKARD. You don't.

Mr. BENTLEY. We wouldn't know--most of--what I am saying i that I think if they have research of this type and they know about the general guidelines relative to the handling of modified R&D in DNA-modified material, they would more than likely come to the agency and ask whether or not it would be useful for them to participate, to get a review. We would encourage them to be linked to an IBC, an

APPENDIX 7

DON FUQUA, Florida, CHAIRMAN

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TOM LEWIS, Florida
DON RITTER, Pennsylvania
SID W. MORRISON, Washington
RON PACKARD, California
JAN MEYERS, Kansas
ROBERT C. SMITH, New Hampshire
PAUL B. HENRY, Michigan
HARRIS W. FAWELL, Illinois
WILLIAM W. COBEY, JR., North Carolina
JOE BARTON, Texas
D. FRENCH SLAUGHTER, JR., Virginia
DAVID S. MONSON, Utah

HAROLD P. HANSON
Executive Director
ROBERT C. KETCHAM
General Counsel
JOYCE GROSS FREIWALD
Republican Staff Director

August 12, 1986

Dr. William Gartland, Director
Recombinant DNA Advisory Committee
National Institutes of Health
Building 31, Room 3B10
Bethesda, MD 20892

Dear Dr. Gartland:

Enclosed is a copy of the transcript from the July 23, 1986 hearing at which you testified before the Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources, Agriculture Research and the Environment, and the Subcommittee on Science, Research and Technology on the federal regulation of biotechnology. Attached to the transcript are instructions for submitting requests for changes or clarification. Please review these instructions and the enclosed transcript of your remarks carefully. Your copy of the transcript, together with any written requests for changes, should be returned by September 3, 1986, to:

Dr. Irene B. Glowinski, Science Consultant
Committee on Science and Technology
822 House Office Building Annex #1
Washington, D.C. 20515-6307

The Subcommittees have developed some further questions as a result of the hearing. We would appreciate it if you would submit your responses to these questions when you return your transcript.

The functions of Institutional Biosafety Committee's (IBC's) with respect to USDA funded biotechnology research are outlined on p. #23390 of the June 26, 1986 Federal Register notice.

-- Is it your impression that the IBC will be the level at which the most rigorous oversight will be given to biotechnology based research proposals?

-- Do you think that IBC's, as they are presently devised, will be capable of adequately carrying out these responsibilities?

-- Are these functions, outlined for the IBC's, in accordance with the role the NIH-RAC had defined for IBC's?

Dr. William Gartland
August 12, 1986
Page Two

Your testimony at the hearing was extremely valuable to the Members, and we wish to extend our thanks for your participation and service to the Committee.

Sincerely,

Doug Walgren Harold Volkmer

James H. Scheuer
Member of Congress

Doug Walgren
Member of Congress

Harold L. Volkmer
Member of Congress

IG/lcg

COMMITTEE ON SCIENCE AND TECHNOLOGY

Subcommittee on Investigations and Oversight

Subcommittee on Natural Resources, Agriculture Research and the Environment

Subcommittee on Science, Research and Technology

Additional Questions

Q: Is it your impression that the IBC will be the level at which the most rigorous oversight will be given to biotechnology based research proposals?

A: It is my impression that the IBC will be the level at which the most rigorous oversight will be given to proposals which fall under Subpart - .203, "Agricultural Research that Requires IBC Notification at Initiation - Category 2," and to some proposals under Subpart - .204, "Agricultural Research that Requires IBC Approval and USDA Registration Before Initiation - Category 3" of the Proposed USDA Guidelines for Biotechnology Research. Experiments which fall under Subpart - .205 "Agriculture Research that Requires USDA and IBC Approval Before Initiation: Release of Organisms - Category 4," will receive rigorous review at both the IBC and USDA levels.

Q: Do you think that IBC's, as they are presently devised, will be capable of carrying out these responsibilities?

A: I believe that IBCs will be able to carry out the responsibilities assigned to them by the Proposed USDA Guidelines for Biotechnology Research.

Q: Are these functions, outlined for the IBC's, in accordance with the role the NIH-RAC had defined for IBC's?

A: The functions assigned to the IBCs in Subpart - .404 of the proposed USDA Guidelines for Biotechnology Research are very similar to functions assigned to IBCs by Section IV-B-3 of the NIH Guidelines.

APPENDIX 8

CHARTER

BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE
OF THE
FEDERAL COORDINATING COUNCIL
FOR SCIENCE, ENGINEERING, AND TECHNOLOGY

PURPOSE

The Domestic Policy Working Group on Biotechnology has determined that in the area of biotechnology with its rapid growth of scientific discovery, scientific issues of interagency concern will arise frequently and need to be communicated among the various agencies involved with reviews of biotechnology applications. The Federal Coordinating Council for Science, Engineering, and Technology (FCCSET) established by 42 U.S.C. 6651 is an interagency science committee chaired by the Director of the Office of Science and Technology Policy with the mission of coordinating science activities affecting more than one agency. Committees may be established under FCCSET for addressing particular science issues. Thus, the Biotechnology Science Coordinating Committee (BSCC) is established to provide formally an opportunity for interagency science policy coordination and guidance and for the exchange of information regarding the scientific aspects of biotechnology applications submitted to federal research and regulatory agencies for approval.

FUNCTIONS

The BSCC will coordinate interagency review of scientific issues related to the assessment and approval of biotechnology research applications and biotechnology product applications and post-marketing surveillance when they involve the use of recombinant RNA, recombinant DNA, cell fusion or similar techniques. The BSCC will:

(a) Serve as a coordinating forum for addressing scientific problems, sharing information, and developing consensus;

(b) Promote consistency in the development of Federal agencies' review procedures and assessments;

(c) Facilitate continuing cooperation among Federal agencies on emerging scientific issues; and,

(d) Identify gaps in scientific knowledge.

AUTHORITY

To accomplish these functions the BSCC is authorized to:

(a) Receive documention from agencies necessary for the performance of its functions;

(b) Conduct analyses of broad scientific issues that extend beyond those of any one agency;

(c) Develop generic scientific recommendations that can be applied to similar, recurring applications;

(d) Convene workshops, symposia, and generic research projects related to scientific issues in biotechnology; and

(e) Hold periodic public meetings.

MEMBERS AND CHAIRMAN

The BSCC includes the following initial members:

- Department of Agriculture
  - Assistant Secretary for Marketing and Inspection Services
  - Assistant Secretary for Science and Education
- Department of Health and Human Services
  - Commissioner Food and Drug Administration
  - Director National Institutes of Health
- Environmental Protection Agency
  - Assistant Administrator for Pesticides and Toxic Substances
  - Assistant Administrator for Research and Development
- National Science Foundation
  - Assistant Director for Biological, Behavioral & Social Sciences

The BSCC is chaired by the Assistant Director for Biological, Behavioral and Social Sciences of the National Science Foundation and the Director of the National Institutes of Health on a rotating basis.

ADMINISTRATIVE PROVISIONS

(a) The BSCC will report to FCCSET through the Chair.

(b) Meetings of the BSCC shall be held periodically. Some public meetings will be held.

(c) Confidential business information and proprietary information shall be protected under the confidentiality requirements of each member agency.

(d) Subcommittees and working groups, with participation not restricted to BSCC members or full-time Federal employees, may be formed to assist the BSCC in its work.

(e) All BSCC members will be full-time Federal employees whose compensation, reimbursement for travel expenses and other costs shall be borne by their respective agencies.

(f) Each member of the BSCC shall provide such agency support and resources as may be available and necessary for the operation of the BSCC including undertaking special studies as come within the functions assigned herein.

(g) An Office of Science and Technology Policy staff member will serve as BSCC Executive Secretary.

DURATION

The BSCC shall continue for a period of two years at which time the continuing need for the BSCC will be reviewed prior to its renewal.

DETERMINATION

I hereby determine that the formation of the BSCC is in the public interest in connection with the performance of duties imposed on the Executive Branch by law, and that such duties can be best performed through the advice and counsel of a such a group.

Approved:

October 30, 1985
(Date)

G.A. Keyworth, II, Chairman
Federal, Coordinating Council
for Science, Engineering and
Technology

BIOTECHNOLOGY SCIENCE COORDINATING COMMITTEE
OF THE
FEDERAL COORDINATING COUNCIL
FOR SCIENCE, ENGINEERING, AND TECHNOLOGY

AGREEMENT OF THE MEMBERS

The undersigned members of the BSCC, in order to fully participate in the activities of the BSCC, do hereby agree to: expedite all necessary proper agency clearances for other members so that they can receive proprietary and confidential business information; provide a system to fully protect proprietary and confidential business information; provide such agency support and resources as may be available and necessary for the operation of the BSCC; and, to perform such other duties for the operation of the BSCC as may be necessary to carry out the functions described above.

Raymond D. Lett — 11-13-85
Assistant Secretary for Marketing and Inspection Services, Department of Agriculture — Date

Orville G. Bentley — Nov. 8, 1985
Assistant Secretary for Science and Education, Department of Agriculture — Date

Frank E. Young — NOV 6 1985
Commissioner, Food and Drug Administration Department of Health and Human Services — Date

James B. Wyngaarden — Nov 6, 1985
Director, National Institutes of Health Department of Health and Human Services — Date

8 Nov 1985
Assistant Administrator for Pesticides and Toxic Substances Environmental Protection Agency — Date

8 Nov 1985
Assistant Administrator for Research and Development, Environmental Protection Agency — Date

David T. Kingsbury — November 6, 1985
Assistant Director for Biological, Behavioral and Social Sciences, National Science Foundation — Date

APPENDIX 9

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
Building : 31
Room : 3B10
(301) 496- 6051

October 20, 1986

The Honorable Harold L. Volkmer
Chairman
Subcommittee on Investigations
and Oversight
Committee on Science and Technology
House of Representatives
Washington, DC 20515

Dear Mr. Volkmer:

At the July 23 hearing before the Subcommittee on Investigations and Oversight, the Subcommittee on Natural Resources, Agriculture Research and the Environment, and the Subcommittee on Science, Research and Technology, you expressed interest in receiving the National Institutes of Health report on the field testing of a pseudorabies vaccine at Baylor College of Medicine and Texas A & M University. I am pleased to enclose a copy of the final report. Please feel free to contact me if your wish additional information.

Sincerely yours,

William Gartland

William J. Gartland, Jr., Ph.D.
Director
Office of Recombinant DNA Activities
National Institute of Allergy and
Infectious Diseases

Enclosure

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date October 9, 1986

From Director, National Institute of General Medical Sciences

Subject Report of Committee - ACTION

To Director, National Institutes of Health

Attached is the final Report of the Committee which you appointed and asked me to chair, "to review the allegations of violations of the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) in the conduct of field tests of a pseudorabies vaccine at Baylor College of Medicine and/or Texas A & M University."

Your charge to the Committee, dated May 7, 1986, and the Committee membership are found in Attachment A to the Report.

The final Report has eight sections. Sections A and B of the Report provide background and describe how the Report was developed. Section C lists the documents which the Committee reviewed and upon which it based its recommendations. Section D describes the relevant sections of the NIH Guidelines. Section E reviews the questions considered by the Committee. Section F contains the Committee conclusions. A draft document containing these six sections of the Committee Report was sent for comment to Dr. Saul Kit and others; Section G gives the Committee's responses to the comments received. Section H contains our recommendations.

If you wish to discuss the Report, Dr. Talbot and I would be pleased to meet with you for this purpose.

In summary, we found ambiguities in the NIH Guidelines, both in regard to whether the pseudorabies vaccine used in the field test consisted of "recombinant DNA molecules," and whether the field test constituted "deliberate release into the environment" (see Report, pages 5-8). In spite of these ambiguities, we found Dr. Saul Kit "remiss in not having consulted with the Institutional Biosafety Committee (IBC) at Baylor College of Medicine and in not seeing to it that the IBC at Texas A & M University was consulted prior to conducting the Maddox Farm field test" (see Report, page 10).

Our recommendations to you (see Report, pages 15-16) are stated below. We request that you indicate whether or not you concur.

1. That, for the next three years, in addition to all usual required approvals, each future project involving the use of animals on which Dr. Saul Kit (as a member of an Institution which receives any support for

recombinant DNA research from the NIH) is a participating investigator, must be reviewed by that Institution's Biosafety Committee. That Committee must determine whether each such project requires its prior approval and shall report every six months to the NIH Office of Recombinant DNA Activities concerning the actions it has taken on the projects submitted by Dr. Kit.

Concur JB Wyngaarden Non-concur ____________

Date 10-15-86

2. That, for each ongoing project involving the use of animals, on which Dr. Saul Kit is a participating investigator, the NIH Office of Recombinant DNA Activities, after consultation with the Baylor College of Medicine Subcommittee on Recombinant DNA, and with the Institutional Biosafety Committee of any collaborating institution, shall determine the appropriate action to be taken.

Concur JB Wyngaarden Non-concur ____________

Date 10-15-86

3. That no further action be taken in regard to Baylor College of Medicine or Texas A & M University, as institutions.

Concur JB Wyngaarden Non-concur ____________

Date 10-15-86

4. That the NIH Recombinant DNA Advisory Committee recommend clarification of the NIH Guidelines as to: (1) whether a molecule is to be considered as a "recombinant DNA molecule" when an initial construction of a recombinant DNA molecule outside living cells is followed by a second recombinational event which takes place within a living cell resulting in a molecule which contains no foreign DNA and/or no ligation junctions; and (2) what constitutes "deliberate release into the environment."

Concur JB Wyngaarden Non-concur ____________

Date 10-15-86

5. That the NIH Office of Recombinant DNA Activities (ORDA) write to all Institutional Biosafety Committees (IBCs) registered with ORDA and request them to remind the scientists at their institutions of their responsibilities under the NIH Guidelines for Research Involving Recombinant DNA Molecules. Scientists should be told that they should be very cautious in making their own interpretations of the NIH Guidelines, and when they have questions, should consult with their IBCs. For collaborative research that involves more than one institution, they should be sure that investigators and IBCs at all involved institutions are appropriately consulted.

Concur JBWyngaarden Non-concur ____________

Date 10-15-86

Upon receiving this memorandum back from you indicating your concurrence with the recommendations, I will see to it that: (a) the recommendations are carried out; and (b) copies of the Report and this memorandum are sent to Mr. Lee Rogers (who requested the investigation), all those listed in Attachment B to the Report, and any others who have requested or may request a copy.

Ruth L. Kirschstein
Ruth L. Kirschstein, M.D.

Attachment

October 9, 1986

Report of the Committee to Review Allegations of Violations of the NIH Guidelines for Research Involving Recombinant DNA Molecules in the Conduct of Field Tests of a Pseudorabies Vaccine at Baylor College of Medicine and/or Texas A & M University

A. - Background

On May 7, 1986, Dr. James B. Wyngaarden, Director, National Institutes of Health (NIH), established the above named Committee (the NIH Committee) as described in Attachment A (which includes the roster of Committee members). He charged the Committee "to review the allegations of violations of the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) in the conduct of field tests of a pseudorabies vaccine at Baylor College of Medicine and/or Texas A & M University...and report...whether...a violation of the NIH Guidelines took place and, if so, what action...NIH should take."

B. - Development of This Report

The first Committee meeting was held on May 27, 1986. A second meeting was held on July 8, 1986. Following the third meeting on July 15, 1986, a draft version of this Report was adopted. The draft, dated August 7, 1986, was sent for comment to the individuals listed in Attachment B. Comments received were considered by the Committee at its fourth meeting on September 17, 1986. Following that meeting a new draft of this Report was sent to all Committee members. They were polled subsequently, and this Report now has the Committee's unanimous endorsement.

C. - Documents Reviewed

The following documents were reviewed by the Committee:

Document I -- Letter of April 28, 1986, from Edward Lee Rogers, attorney, to Richard Lyng, Secretary of Agriculture, and Dr. James B. Wyngaarden, Director of the National Institutes of Health. In this letter (submitted on behalf of the Foundation on Economic Trends, Jeremy Rifkin and Michael W. Fox), Mr. Rogers petitions that "the National Institutes of Health ('NIH') investigate the circumstances of field tests of the [Pseudorabies] vaccine conducted in apparent violation of the NIH Guidelines for Research Involving Recombinant DNA Molecules, ("NIH Guidelines') 49 Fed. Reg. 46266 (1984), as amended, by the Baylor College of Medicine ('Baylor') acting directly and also through Dr. Saul Kit, Professor and Head of the Division of Biochemical Virology at Baylor, and his associates....The field test in question was conducted at the Maddox Farm."

Document II -- NIH Guidelines for Research Involving Recombinant DNA Molecules. The NIH Guidelines were originally issued in 1976 and have been revised many times since with complete republication in the Federal Register occurring periodically. The version of the NIH Guidelines in effect at the time of inoculation of pigs with pseudorabies vaccine at the Maddox Farm was published in the Federal Register on June 1, 1983 (48 FR 24556). None of the changes in the NIH Guidelines made since June 1, 1983, are germane to the issues in this case.

Document III -- Environmental Assessment and Finding of No Significant Impact, prepared by the U.S. Department of Agriculture for "the license issued by the United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, under the Virus-Serum-Toxin Act to TechAmerica Group, Inc., to manufacture, market, and distribute a recombinant derived pseudorabies virus vaccine for the purpose of preventing pseudorabies virus infection in swine," dated April 21, 1986.

Document IV -- Letter of April 25, 1986, from James Wild, Chairman, Institutional Biosafety Committee (IBC), Texas A & M University, to Dr. William Gartland, Jr., Director, Office of Recombinant DNA Activities, NIH. The letter has as attachments two published scientific articles, i.e., "Attenuated Properties of Thymidine Kinase-negative Deletion Mutant of Pseudorabies Virus," by S. Kit, M. Kit, and E. C. Pirtle, in Am. J. Vet. Res. 46, 1359, 1985 (Document IV-A), and "Immunization of Pregnant Pigs in a Quarantined Swine Herd with a Thymidine Kinase Deletion Mutant of Pseudorabies Virus," by S. Kit, M. Kit, B. Lawhorn, and S. McConnell in "High Technology Route to Viral Vaccines," 1985, American Society for Microbiology, Eds. G. R. Dreesman, J. G. Bronson and R. C. Kennedy, pages 82-99 (Document IV-B). The latter paper describes the segment of the Maddox Farm field test in which pigs were inoculated in June 1984.

Document V -- Letter of May 6, 1986, from Alan J. Garber, Chairman, Subcommittee on Recombinant DNA, Biohazard Safety Committee, Baylor College of Medicine, to Dr. Gartland, with attachments.

Document VI -- U.S. Patent 4,514,497, issued April 30, 1985, "Modified Live Pseudorabies Viruses," inventors: Malon Kit and Saul Kit.

Document VII -- U.S. Department of Agriculture Veterinary Services Memorandum No. 800.68, "New Biotechnology for Preparation of Animal Biological-Products," dated December 4, 1984.

Document VIII -- Coordinated Framework for Regulation of Biotechnology (Federal Register, June 26, 1986, 51 FR 23302).

Document IX -- Letter of July 11, 1986, from Dr. Saul Kit to Dr. Bernard Talbot, Deputy Director, National Institute of Allergy and Infectious Diseases, with attachments.

Document X -- Letter of August 13, 1986, from Dr. Saul Kit to Dr. Bernard Talbot, with attachment.

Document XI -- Letter of August 20, 1986, from Dr. Bernard Talbot to Dr. Saul Kit, with attachments.

Document XII -- Letter of August 28, 1986, from Dr. Saul Kit to Dr. Bernard Talbot, with attachments.

Document XIII -- Letter of August 22, 1986, from Dr. Bruce Lawhorn to Dr. Bernard Talbot, with attachments.

Document XIV -- Letter of September 4, 1986, from Dr. James Wild to Dr. Bernard Talbot with attachments.

Document XV -- Letter of September 5, 1986, from Dr. Alan J. Garber to Dr. Bernard Talbot.

Document XVI -- Minutes of the April 22, 1986, meeting of the Texas A & M University Institutional Biosafety Committee.

D. - Relevant Sections of the NIH Guidelines

The NIH Committee concluded that the following sections of the NIH Guidelines are relevant to this review:

1 - Section I-C, "General Applicability," which states:

> "The Guidelines are applicable to all recombinant DNA research within the United States or its territories which is conducted at or sponsored by an Institution that receives any support for recombinant DNA research from the National Institutes of Health (NIH)."

2 - Section I-B, "Definition of Recombinant DNA Molecules," which states:

> "In the context of these Guidelines, recombinant DNA molecules are defined as either: (i) Molecules which are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or (ii) DNA molecules that result from the replication of those described in (i) above."

3 - Section III-A, "Experiments that Require RAC Review and NIH and IBC Approval Before Initiation," which includes as a subclass, in Section III-A-2:

> "Deliberate release into the environment of any organism containing recombinant DNA...."

4 - Section III-D, "Exempt Experiments," which in Section III-D-2 exempts from the NIH Guidelines those recombinant DNA molecules:

> "that consist entirely of DNA segments from a single nonchromosomal or viral DNA source...."

This exemption, however, is overridden by the following statement which appears under Section III:

> "If an experiment falls into both class III-A and one of the other classes, the rules pertaining to class III-A must be followed."

Thus in the case of "deliberate release into the environment," which falls under Class III-A, the rules pertaining to Class III-A (i.e., required prior RAC review and NIH and IBC approval) override any exemption which would hold for work with these same molecules in a contained laboratory.

E. - Questions Considered by the NIH Committee

1 - Was the Field Test Conducted at or Sponsored by an Institution That Receives Any Support for Recombinant DNA Research from the NIH? (Guidelines Section I-C)

The publication describing the Maddox Farm field test (Document IV-B), lists as the authors: S. Kit and M. Kit (and gives their affiliation as Baylor College of Medicine) and B. Lawhorn and S. McConnell (and gives their affiliation as Texas A & M University System). This provides documentation that this field test was "sponsored by" these two institutions. Both Baylor College of Medicine and Texas A & M University receive NIH funds for recombinant DNA research. Therefore the NIH Committee concludes that the field test was indeed sponsored by institutions that receive NIH support for recombinant DNA research.

2 - Did the Vaccine Which Was Administered to the Pigs in the Field Test Consist of "Recombinant DNA Molecules"? (Guidelines Section I-B)

The pseudorabies vaccine virus administered to the pigs in the field test is called "PRV(BUK-dl3)." It was derived from the Bucharest vaccine strain [PRV(BUK)]. The Bucharest vaccine strain is described by Dr. Kit as follows:

> "The Bucharest vaccine strain is a thymidine kinase-positive (TK^+) vaccine strain obtained by conventional genetic engineering techniques, i.e., by genetically altering a PRV field strain through passage (growth) of the virus 100 times in chicken embryos and approximately 600 times in chicken embryo fibroblast cells in culture....This genetic alteration of the virus was found to cause reduction in the number of animals affected by the disease and its severity. Recently, it has been determined that the alteration of the TK^+ Bucharest strain, which alteration results in attenuation, is a 3-4 Kb deletion in the BamHI-12 and KpnI-I portions of the virus DNA. This region of the viral genome encodes the glycoprotein gI gene. As a result of the deletion, the altered virus fails to produce the gI glycoprotein. The gI glycoprotein is believed to facilitate the entry/egress, relative to the infectivity, of PRV from host cells and/or the spread of the virus from the site of infection to the central nervous system. Viruses lacking the gI gene are believed to be impaired in their ability to carry out these functions....Over 23 million vaccine doses of the Bucharest strain have been marketed in the United States in the last 8 years." (Document IX, pages 1-2)

The derivation of PRV(BUK-dl3) from PRV(BUK) is described as follows in the April 18, 1986, Memorandum from Inquiry Panel to Dr. Garber (an Attachment to Document V):

> "The pseudorabies vaccine virus, PRV(BUK-dl3), was derived by Dr. Kit from an established vaccine strain of PRV [PRV(BUK)]. This derivation involved engineering a 148-basepair deletion (using recombinant DNA technology) in a cloned fragment of PRV DNA (taken from the homologous virus) containing the coding sequences for thymidine kinase (TK). Rabbit kidney cells were transfected with intact PRV DNA and the nonreplicating fragment bearing the TK deletion. The vaccine isolate [PRV(BUK-dl3)] was drug-selected from among the progeny viruses produced by the transfected cells; it had incorporated the TK gene deletion by homologous recombination within the cell."

The development of the PRV(BUK-dl3) virus vaccine is shown schematically in Figure One. In its derivation, two recombinant plasmids were used. One, "recombinant plasmid pBB11" [(a) in Figure One], is described in Document IV-A as "a pBR322 derivative containing an insert of the BamHI-11 fragment of TK^+PRV(BUK)." The second, plasmid pBB11 dlP4 [(b) in Figure One], is described as "a derivative of pBB11 with a deletion of about 148 base pairs in the coding region of the TK gene." Both plasmids clearly fall under the definition of "recombinant DNA" in Section I-B of the NIH Guidelines in that they are molecules "constructed outside living cells by joining natural...DNA segments" [in both cases, a fragment of PRV(BUK)] "to DNA molecules that can replicate in a living cell" (namely, plasmid pBR322).

These two plasmids were used in the derivation of PRV(BUK-dl3) by cotransfecting living cells with both viral DNA and plasmid and selecting pseudorabies viral recombinants which arose within the cells. In the first transfection procedure (step 2 in Legend for Figure One), the mutagen-induced TK^- derivative of the PRV(BUK) strain, PRV(BUK-5A), was cotransfected into rabbit cells with the plasmid pBB11; a resulting TK^+ pseudorabies virus recombinant was selected. While a recombinant DNA plasmid was used as the source of the TK^+ DNA for this step, no "ligation junction"[1] or foreign DNA was present in the pseudorabies virus thus generated, designated PRV(BUK-5A-R1).

In the second transfection procedure (step 3 in Legend for Figure One), DNA from the PRV(BUK-5A-R1) derivative was cotransfected into rabbit cells with the pBB11 dlP4 plasmid (which contained a TK deletion). Pseudorabies viral recombinants which had acquired the 148 base pair TK deletion from the plasmid were selected and purified. One of these deleted virions, PRV(BUK-dl3), was selected and subsequently used to vaccinate pigs. The genome of this virus was exclusively of pseudorabies virus derivation. However, it did contain a segment of DNA having a 148 base pair deletion in the TK gene, including the deletion junction which it acquired as a result of homologous recombination with pBB11 dlP4 during its propagation in rabbit cells.

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[1] The term "ligation junction" is used to designate the site of joining two DNA segments outside living cells.

The NIH Committee finds two possible sources of ambiguity in these procedures:

a) Does the use of a recombinant DNA molecule as one of the partners in a recombination process taking place within living cells inevitably render the product "recombinant DNA"?

One interpretation of the NIH Guidelines is that where no ligation junctions or foreign DNA are present (as in the product of step 2 in Legend for Figure One), the product should not be considered recombinant DNA. By this interpretation, PRV(BUK-5A-R1) would not be considered a recombinant DNA molecule. An alternative interpretation would conclude that PRV(BUK-5A-R1) is a recombinant DNA molecule because one of the partners in the recombination process, pBB11, was a plasmid constructed by recombinant DNA technology.

b) Does the construction of a deletion by recombinant DNA methods and the subsequent incorporation of that deletion into a virus result in "recombinant DNA"? In this case, the deletion was constructed by ligating together restriction enzyme treated recombinant plasmid DNA outside living cells. Subsequently (step 3 in Legend for Figure One), this deletion was transferred to the pseudorabies virus genome by homologous recombination within living cells. No foreign DNA was introduced, however.

Historically, such deletion derivatives have been considered as recombinant DNA molecules both by the NIH and its Recombinant DNA Advisory Committee, e.g., in consideration of applications involving "ice minus" Pseudomonas syringae and Erwinia herbicola. Furthermore, it was noted by the NIH Committee, although the Maddox Farm field test was not submitted for prior review to either the Baylor College of Medicine Subcommittee on Recombinant DNA or the Texas A & M University Institutional Biosafety Committee, that when these two committees did consider the field test after it had already been initiated, each came to the same conclusion, i.e., in considering the question, "is the viral vaccine a recombinant molecule?" a majority of the members of the Texas A & M University IBC voted yes (Document XVI), and a majority of the Baylor College of Medicine Subcommittee on Recombinant DNA concluded that "Dr. Kit's vaccine virus represented a recombinant DNA molecule" (Minutes of the April 28, 1986, Special Meeting of the Baylor College of Medicine Subcommittee on Recombinant DNA, an Attachment to Document V). However, one member of the latter Committee concluded, "Dr. Kit's procedures utilized classical virological marker rescue methods, predicated on recombination between viral DNA sequences within an infected cell. This member noted that the fact that a recombinant DNA step was used in an early stage of research that did not introduce any foreign DNA sequences may not necessarily make the end product a recombinant DNA organism." The NIH Committee concludes that there is ambiguity in the NIH Guidelines on this point.

The NIH Committee suggests that the NIH Recombinant DNA Advisory Committee consider[2] this issue and recommend a clarification of the NIH Guidelines in regard to whether a molecule is to be considered as a "recombinant DNA molecule" when an initial construction of a recombinant DNA molecule outside living cells is followed by a second recombinational event which takes place within a living cell resulting in a molecule which contains no foreign DNA and/or no ligation junctions.

3 - Did the Field Test of the Pseudorabies Virus Vaccine Involve "Deliberate Release Into the Environment of An Organism Containing Recombinant DNA"? (Guidelines Section III-A-2)

Although Section III-A-2 of the NIH Guidelines uses the phrase "deliberate release into the environment," it is not defined. However, the Baylor College of Medicine Subcommittee on Recombinant DNA unanimously concluded that the Maddox Farm field test "constituted release of the vaccine virus into the environment" (Minutes of the April 28, 1986, Special Meeting of the Baylor College of Medicine Subcommittee on Recombinant DNA, an Attachment to Document V). The Texas A & M University IBC in considering the question, "Do these studies [inoculation of tk$^-$ deletion viral vaccines into large animal systems] constitute potential environmental release?" voted unanimously yes (Document XVI).

In their discussion, members of the NIH Committee differed as to where they would draw the line between finding that organisms containing recombinant DNA to be used in an experiment are "contained" and finding that "deliberate release into the environment" would occur. The NIH Committee concluded that there are ambiguities both in regard to the phrase "release into the environment" and the word "deliberate."

The NIH Committee also notes that there appear to be differing opinions among Federal agencies. Document IV points out that the investigators performing the Maddox Farm field test cited the U.S. Department of Agriculture Veterinary Services Memorandum No. 800.68 (Document VII) in which the following statement appears:

> "In normal husbandry and laboratory practices, veterinary biological products are not considered to be released into the environment."

Furthermore, a Federal interagency group has commented on the difficulties in defining "release into the environment." The Biotechnology Science Coordinating Committee (BSCC) consists of senior officials from the NIH, Food and Drug Administration (FDA), Department of Agriculture (USDA), Environmental Protection Agency (EPA), and National Science Foundation (NSF). It recently stated:

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[2] We are aware that the NIH Recombinant DNA Advisory Committee (RAC) is already considering this issue and that it was discussed both at the September 5, 1986, meeting of the RAC Working Group on Definitions and at the September 29, 1986, meeting of the full RAC.

> "The BSCC is attempting to define what constitutes 'release into the environment.' ...The concept of 'containment' has traditionally been used to describe physical conditions which severely limit release (for example, a contained laboratory fermentation facility). Containment can also be 'biologic' because the ability of an organism to reproduce, exchange genetic information, or become established can be effectively limited biologically... While the concept of physical containment may imply the high containment conditions found in certain laboratories and greenhouses, in agricultural practice many simpler effective barriers are routinely used; these include microplots for soil bacteria and fungi, paddocks for noninfective animals, and removing or covering the reproductive parts of plants and animals. Release into the environment, for the time being, will have somewhat varying definitions for the regulatory and research review of the different agencies." (Document VIII, page 23307)

In view of these ambiguities, the NIH Committee recommends that the NIH Recombinant DNA Advisory Committee consider[3] this issue and recommend a clarification of the NIH Guidelines in this regard.

In the particular case of the pseudorabies virus vaccine, there was no opportunity, prior to the field test, for the NIH to have reached a decision as to whether it would have constituted "deliberate release into the environment." In this case, field tests have already been done and data are available from them. Upon review of the data, the U.S. Department of Agriculture concluded:

> "In summary, these studies clearly demonstrate the stability of the vaccine virus and its inability to be transmitted. A low incidence of nasal excretion of recombinant derived TK^- deleted PRV occurred after intramuscular inoculation of nursing piglets. The titer was low (less than 60 $TCID_{50}$) and only TK^- virus was excreted. This nasally excreted vaccine virus could not be passaged intranasally to other susceptible piglets. These findings are consistent with the characteristics of the conventional modified live PRV from which it was derived." (Document III, page 21)

The NIH Committee concludes that, based on the finding of nasal excretion in these field tests, there was evidence of minimal "release into the environment."

In addition to discussing the above three questions, the NIH Committee noted the findings of the U.S. Department of Agriculture in regard to this pseudorabies vaccine. The USDA Environmental Assessment and Finding of No Significant Impact (Document III) deals with the license which USDA issued to "manufacture, market, and distribute" the pseudorabies virus vaccine and considers the Maddox Farm field test as well as other field tests and other data concerning the vaccine. The NIH Committee finds no reason to question the conclusion which is:

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[3] We are aware that the NIH Recombinant DNA Advisory Committee (RAC) is already considering this issue and that it was discussed both at the September 5, 1986, meeting of the RAC Working Group on Definitions and at the September 29, 1986, meeting of the full RAC.

> "In conclusion, the new recombinant derived pseudorabies modified live virus vaccine was found to be pure, safe, potent, and efficacious by USDA's Veterinary Services. It was produced according to regulations and standards, and adequately tested. The vaccine is needed for the prevention and control of Pseudorabies. To date, no adverse reactions, or adverse impacts on the environment resulting from the administration of the vaccine have been reported to or observed by USDA's field veterinarians. Data and other information available to the Department, as described in this document, support the finding of no significant impact." (Document III, page 25)

F. - Conclusions

In summary, the NIH Committee considered the following three questions: (1) Was the field test "conducted at or sponsored by an Institution that receives any support for recombinant DNA research from the National Institutes of Health;" (2) Did it involve "recombinant DNA molecules;" and (3) Did it involve "deliberate release into the environment"? If the answers to all three questions were "yes," then according to the NIH Guidelines such a field test should have had "RAC review and NIH and IBC approval before initiation." In fact the investigators did not submit the plans for the field test for prior review and approval to either NIH or the IBCs at Baylor College of Medicine or Texas A & M University.

The NIH Committee finds that the field test was indeed "conducted at or sponsored by an Institution that receives any support for recombinant DNA research from the National Institutes of Health." Answers to the questions of whether the vaccine contained "recombinant DNA molecules" or whether the field test involved "deliberate release into the environment" are not clear because of ambiguities in the language of the NIH Guidelines. These ambiguities have not been at issue when research has been confined to the laboratory because recombinant DNA molecules consisting "entirely of DNA segments from a single nonchromosomal or viral DNA source" are exempt from the NIH Guidelines (Section III-D-2) when constructed and handled in the laboratory with no "deliberate release." In regard to whether the vaccine contained "recombinant DNA molecules," the NIH Committee notes that the NIH Recombinant DNA Advisory Committee and the NIH have in the past considered similarly derived molecules to be "recombinant DNA." In regard to whether the Maddox Farm field test involved release into the environment, the NIH Committee found that based on the finding of nasal excretion there was evidence of minimal release into the environment. The NIH Committee believes that, at a minimum, Dr. Kit, an experienced scientist, should have consulted with the IBCs before proceeding to field test his vaccine.

The NIH Committee finds Dr. Saul Kit to be the "principal investigator" (PI) and senior scientist for the "project" spanning the development of the PRV(BUK-dl3) vaccine through its laboratory and field testing.

Despite ambiguities in the NIH Guidelines, the NIH Committee finds Dr. Kit remiss in not having consulted with the Institutional Biosafety Committee (IBC) at Baylor College of Medicine and in not seeing to it that the IBC at Texas A & M University was consulted prior to conducting the Maddox Farm field test. In this conclusion we are in agreement with the Subcommittee on Recombinant DNA of the Baylor College of Medicine which stated:

> "The Subcommittee further finds that Dr. Kit should have sought the advice and approval of the Subcommittee in interpreting NIH Guidelines prior to the initiation of the field tests." (Document V)

and the Texas A & M University IBC which stated:

> "It is the belief of the IBC that the determination of deliberate release is not the option of the PI and any 'potential' release must be evaluated by the IBC, NIH and RAC reviews." (Document IV)

G. - Response to Comments

As noted in Section B of this Report, a draft (dated August 7, 1986) of Sections A through F of this Report was sent for comment to the individuals listed in Attachment B to this Report. Comments were received from: Dr. Saul Kit, Baylor College of Medicine (Document XII); Dr. Bruce Lawhorn, Texas A & M University (Document XIII); Dr. James Wild, Chairman, Institutional Biosafety Committee, Texas A & M University (Document XIV); and Dr. Alan Garber, Chairman, Subcommittee on Recombinant DNA, Biohazard Safety Committee, Baylor College of Medicine (Document XV). Additional information was provided upon request by Texas A & M University (Document XVI). After analysis of these documents, the NIH Committee made certain changes in Sections A through F of this Report. In this Section of the Report, the NIH Committee discusses other aspects of Documents XII through XV.

1 - Comments Concerning Whether the Field Test Was Sponsored by an Institution That Received Support for Recombinant DNA Research From the NIH

Letters from both Dr. James Wild, Chairman, Institutional Biosafety Committee, Texas A & M University, and Dr. Alan Garber, Chairman, Subcommittee on Recombinant DNA, Biohazard Safety Committee, Baylor College of Medicine, objected to the NIH Committee conclusion that the Maddox Farm was "sponsored by" these two institutions.

Dr. Wild wrote:

> "It is inappropriate to state that this research was sponsored by Texas A & M University. Drs. B. Lawhorn and S. McConnell did list the Texas Agricultural Extension Service and Texas A & M University in their publication of this work. However, no permission was ever

> given to perform this work and the funding for this research was provided from non-university sources." (Document XIV)

Dr. Garber wrote:

> "The evidence clearly indicates that none of the experimentation under investigation as performed by Dr. Kit was performed at Baylor College of Medicine per se, nor was any responsible party at Baylor College of Medicine aware of such experimentation. The use of the term 'sponsored by' Baylor College of Medicine implies a degree of active participation and knowledge regarding such experimentation which is not supported by the facts....We, therefore, object strongly to the impression produced by the draft report that Baylor knowingly participated in or sponsored such experimentation and may have supported it with foreknowledge. Furthermore, we therefore respectfully request that the use of the terms 'sponsored by' or 'at Baylor College of Medicine' be deleted from the final report of the committee, since such is contrary to the facts of the matter." (Document XV)

In interpreting whether the NIH has jurisdiction over this case, the NIH Committee stands with its finding that the field test was "sponsored by" these institutions, as the term "sponsored by" is used in the NIH Guidelines. This is based on the fact that published results of the Maddox Farm field test list the affiliations of the authors as Baylor College of Medicine and Texas A & M University. The NIH Committee finds that both Baylor College of Medicine and Texas A & M University, as institutions, were without fault in this case. The field test was begun without the investigators requesting prior approval from the Institutional Biosafety Committees. Upon learning that the field test had begun, both institutions acted responsibly and appropriately in investigating the case and providing clear reports to the NIH.

2 - Comments Concerning Whether the Field Test Involved "Recombinant DNA Molecules"

In Section E-2 of this Report, the members of the NIH Committee reviewed the issue of whether the vaccine which was administered to the pigs in the Maddox Farm field test consisted of "recombinant DNA molecules." Dr. Kit (Document XII, page 6) continues to state that "it is clear that PRV(BUK-dl3) is not a 'recombinant DNA molecule.'" In Documents X and XII, he cites documents other than the NIH Guidelines which define "recombinant DNA" as involving the joining together of DNA segments from different organisms. He then concludes that "since PRV(BUK-dl3) only contains PRV DNA sequences, i.e., it does not contain DNA sequences for another organism, it is clear that PRV(BUK-dl3) is not a 'recombinant DNA molecule.'"

The NIH Committee disagrees with Dr. Kit and holds that for a determination as to whether there has been a violation of the NIH Guidelines, the definition of "recombinant DNA" which appears in those Guidelines must be used. While we conclude that there is ambiguity in this regard, we hold that there should have been prior consultation with the local Institutional Biosafety Committees.

Dr. Kit (in Document XII) cites, a number of times, a statement by Dr. Bernard Talbot, of NIH, which appeared in the Federal Register on January 5, 1984, i.e. that "two pieces of DNA spliced together outside living cells constitute 'recombinant DNA' and fall under the Guidelines, but if the same two pieces of DNA were spliced together within a living cell they would not be considered 'recombinant DNA' and therefore, would not currently fall under the Guidelines." Dr. Kit (Document XII, page 6) claims that this statement "clearly demonstrate that the tk^- deletion mutant, PRV(BUK-dl3), was not considered by him [Dr. Talbot] as a 'recombinant DNA molecule.'"

This is not correct. In Section E-2 of this Report we note that in "the development of the PRV(BUK-dl3) virus vaccine...two recombinant plasmids were used....pBB11...[and] pBB11 dlP4....Both plasmids clearly fall under the definition of 'recombinant DNA' in Section I-B of the NIH Guidelines." (In all his communications, Dr. Kit has not contested that these are "recombinant DNA molecules.") Dr. Talbot's January 5, 1984, statement was included with a series of questions issued for public comment prior to discussion by the RAC. It was based on the definition of "recombinant DNA molecules" in the NIH Guidelines which specifies "molecules which are constructed outside living cells." Dr. Talbot's January 5, 1984, statement means that if molecules identical to pBB11 or pBB11 dlP4 had been constructed inside living cells instead of outside living cells, those molecules would not be considered "recombinant DNA." That statement is not applicable to PRV(BUK-dl3) where, as noted in Section E-2 of this Report, the initial construction of recombinant DNA molecules outside living cells was followed by subsequent recombinational events which took place within living cells resulting in a different molecule. Dr. Talbot's statement did not mean that passage of recombinant DNA molecules through living cells makes them non-recombinant DNA molecules.

Dr. Kit (Document XII, page 6) cites a Federal Register notice of August 15, 1986, which published for public comment "amendments to Section III-A-2 of the NIH Guidelines proposed by Dr. Susan Gottesman seeking to explicitly exclude from RAC and IBC review...deletion derivatives." Dr. Kit (Document XII, page 7) states that "these proposed clarifications...clearly indicate that, historically, the tk^- deletion mutant, PRV(BUK-dl3), was not considered to be an organism containing recombinant DNA, as heretofore defined in the NIH Guidelines."

The NIH Committee disagrees with Dr. Kit's interpretation. Rather than concluding, as does Dr. Kit, that this shows that historically PRV(BUK-dl3) was not considered to be an organism containing recombinant DNA, we conclude that this future change in the NIH Guidelines was proposed precisely because historically such deletion derivatives have indeed been considered as "recombinant DNA molecules." The August 15, 1986, Federal Register notice, which is a proposed amendment to the NIH Guidelines, not a clarification of the current Guidelines, if adopted, would not change the status of deletion derivatives such as PRV(BUK-dl3) as to whether they are or are not "recombinant DNA molecules," but would change registration and review requirements for certain types of experiments using such deletion derivatives.

Dr. Kit (Document XII, page 7) states, "Furthermore, PRV(BUK-dl3) is not an 'intergeneric organism (new organism)' as the definition is formulated by the Biotechnology Science Coordinating Committee (see Federal Register, Vol. 51, No. 123, page 23303 *et seq.*) and thus is exempt from special regulation. This fact likewise demonstrates that historically deletion derivatives have not been considered to be 'recombinant DNA.'"

The NIH Committee agrees that PRV(BUK-dl3) would not be considered an "intergeneric organism (new organism)" under this definition. However, the same *Federal Register* notice which gives this definition (51 FR 23303 *et seq.*) indicates that this in no way changes the definitions in the NIH Guidelines. Again we cannot understand how Dr. Kit can contend that this *new* definition, first published on June 26, 1986, applies to what has been considered *historically* to be "recombinant DNA."

In Section E-2 of this Report, the NIH Committee states, "Historically, such deletion derivatives have been considered as recombinant DNA molecules both by the NIH and its Recombinant DNA Advisory Committee, e.g., in consideration of applications involving 'ice minus' *Pseudomonas syringae* and *Erwinia herbicola*." Dr. Kit (Document XII) replies that the ice-minus cases are not appropriate historical precedents since the ice-minus strains contained "insertions of foreign DNA" (Document XII, page 5) as well as deletions.

The NIH Committee notes that in the original proposal (dated September 17, 1982) submitted to the NIH by Drs. Lindow and Panopoulos requesting approval to field test ice-minus bacteria, they proposed "to construct...various types of 'flagged' deletions having specific DNA sequences or segments physically linked to them." This proposal was not approved by the NIH. In a revised proposal (dated March 8, 1983), Drs. Lindow and Panopoulos wrote, "It is desirable to monitor the survival and dissemination of the mutant bacteria....This is only possible if the mutant strains carry a selectable marker so that they can be readily reisolated from plant and soil material....We wish to clarify certain apparent misunderstandings regarding the antibiotic resistance mutants of ina$^-$ deletion derivatives discussed in our earlier application to RAC: (a) The antibiotic resistance mutations will be *spontaneous mutations*, not recombinant constructions or other types of gene addition." This revised proposal was unanimously recommended for approval by the NIH Recombinant DNA Advisory Committee (RAC) and subsequently approved by NIH. The NIH Committee believes that the ice-minus case does indeed represent a relevant historical precedent for the pseudorabies virus vaccine case.

3 - Comments Concerning Whether the Field Test Involved "Deliberate Release Into the Environment"

Dr. Kit (Document XII, page 1) states that the PRV(BUK-dl3) vaccine "was not 'deliberately released into the environment.'" He states (Document XII, page 4) that, "it was well established *prior* to the vaccination that: (a) the host animal served as both physical and biological containment of the virus; i.e., prior to the vaccination it was known from pilot experiments that vaccinated swine did not shed and transmit the virus to other animals and the virus does not cause disease in vaccinated swine, cattle, or lambs; and (b) the Maddox farm served as a physical containment because it was a *quarantined* farm, with stringent quarantine and containment procedures." Dr. Kit (Document XII, page 2) objects to the NIH Committee's conclusion in Section E-3 of this Report "that, based on the finding of nasal excretion in these field tests, there was evidence of minimal 'release into the environment.'"

In response, the NIH Committee notes again that the Texas A & M University IBC and the Baylor College of Medicine Subcommittee on Recombinant DNA each concluded unanimously that the field test constituted release into the environment. It should be pointed out that the results arising from the conduct of the field tests are not the central issue in this case. The central issue is whether Dr. Kit should have consulted with local Institutional Biosafety Committees *prior* to conducting field tests.

4 - Other Comments

Dr. Kit (Document XII, page 4) states, "The NIH Guidelines state in Section V, Footnote 21, that '[O]ther experiments involving rDNA in human subjects such as...the administration of *vaccines* containing rDNA are not covered by Section III-a-4 of the Guidelines,' i.e., do *not* require IBC review. This exemption, by analogy, would also apply to animal vaccines such as PRV(BUK-dl3)."

The NIH Committee finds that this is a misinterpretation of the NIH Guidelines. Footnote 21 of the NIH Guidelines refers only to Section III-A-4 of the Guidelines which deals with transfer of recombinant DNA into human subjects "in which the intent is to modify stably the genome of cells of a human subject," i.e. human gene therapy. Footnote 21 states that the administration of vaccines to human subjects is not covered under Section III-A-4. This does not mean that such experiments are exempt from IBC review; they would in fact require IBC review if they fall under another Section of the NIH Guidelines requiring such. To then go on and state that "this exemption, by analogy, would also apply to animal vaccines" is a further misinterpretation by Dr. Kit.

Dr. Bruce Lawhorn indicates (Document XIII) that "the Maddox Farm field test is still ongoing and not yet concluded." The NIH Committee has modified its original statement accordingly.

The NIH Committee believes the following quote from Dr. Wild provides a good summary of the case:

> "The use of a live viral vaccine altered by recombinant DNA technologies clearly represents an issue with many complex considerations. When ambiguities exist, it is widely recognized by virtually all members of the scientific community that it is necessary for individual investigators to seek the advice of the local IBC and/or RAC. In this case, the research scientists did not seek advice, consultation or approval from any established authoritative advisory committee or individuals not involved directly in their priority goals. This type of insulary decision making exposes the entire scientific community to emotional claims of personally justified, self-serving biosafety considerations that may be unacceptable by any objective evaluation." (Document XIV)

H. NIH Committee Recommendations

The NIH Committee recommends that the Director, NIH, take the following actions:

1 - Recommendations In Regard to Dr. Saul Kit

a. That, for the next three years, in addition to all usual required approvals, each future project involving the use of animals on which Dr. Saul Kit (as a member of an Institution which receives any support for recombinant DNA research from the NIH) is a participating investigator, must be reviewed by that Institution's Biosafety Committee. That Committee must determine whether each such project requires its prior approval and shall report every six months to the NIH Office of Recombinant DNA Activities concerning the actions it has taken on the projects submitted by Dr. Kit.

b. That, for each ongoing project involving the use of animals, on which Dr. Saul Kit is a participating investigator, the NIH Office of Recombinant DNA Activities, after consultation with the Baylor College of Medicine Subcommittee on Recombinant DNA, and with the Institutional Biosafety Committee of any collaborating institution, shall determine the appropriate action to be taken.

2 - Recommendations In Regard to Baylor College of Medicine and Texas A & M University

The NIH Committee finds that, upon being apprised that the pseudorabies vaccine field tests had begun, both Baylor College of Medicine and Texas A & M University acted promptly and responsibly in investigating the case and providing clear reports to the NIH, i.e. Documents IV and V.

The NIH Committee endorses the following actions by the two Institutions, as stated:

> "The Subcommittee will remind all departmental chairmen that any questions concerning the interpretation of the guidelines or other regulations should be referred to the Subcommittee." (Minutes of April 23, 1986, Meeting of Baylor College of Medicine Subcommittee on Recombinant DNA, an Attachment to Document V)
>
> "Our IBC and the administration have undertaken new efforts to insure that all components of our [Texas A & M] University System (the University, the Agricultural Experiment Station, and the Agricultural Extension Service including off-campus programs) are aware of their responsibilities." (Document IV)

The NIH Committee recommends no further action in regard to Baylor College of Medicine or Texas A & M University.

3 - Recommendations for the National Institutes of Health

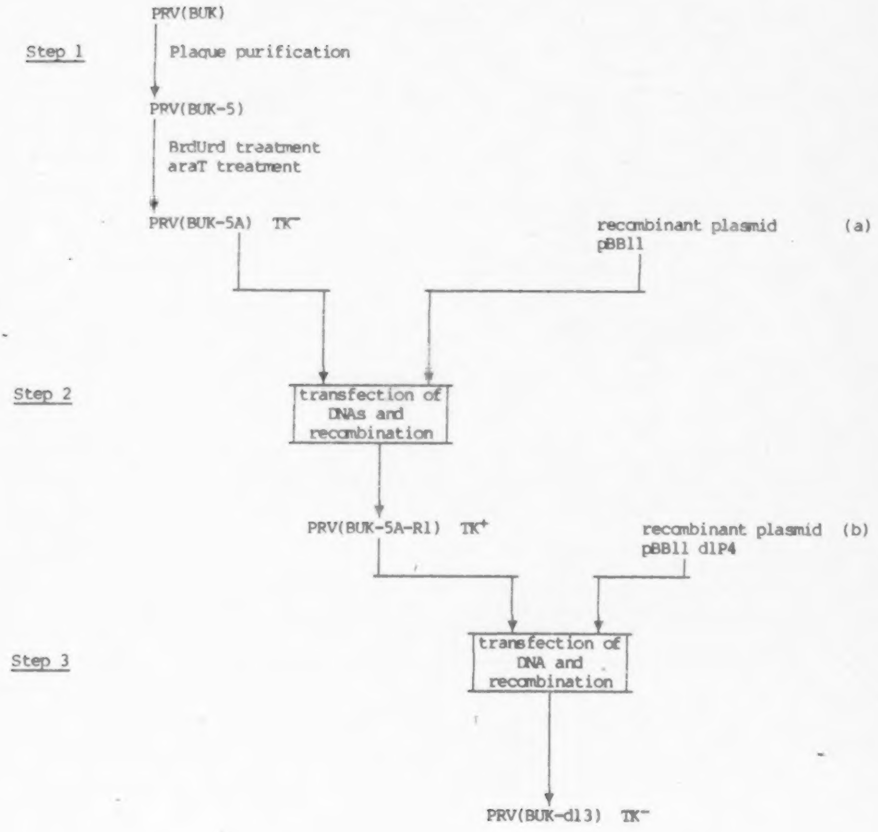
As noted earlier in this report, the NIH Committee recommends that the NIH Recombinant DNA Advisory Committee recommend clarification of the NIH Guidelines as to: (1) whether a molecule is to be considered as a "recombinant DNA molecule" when an initial construction of a recombinant DNA molecule outside living cells is followed by a second recombinational event which takes place within a living cell resulting in a molecule which contains no foreign DNA and/or no ligation junctions; and (2) what constitutes "deliberate release into the environment."

In addition the NIH Committee recommends that the NIH Office of Recombinant DNA Activities (ORDA) write to all Institutional Biosafety Committees (IBCs) registered with ORDA and request them to remind the scientists at their institutions of their responsibilities under the NIH Guidelines for Research Involving Recombinant DNA Molecules. Scientists should be told that they should be very cautious in making their own interpretations of the NIH Guidelines, and when they have questions, should consult with their IBCs. For collaborative research that involves more than one institution, they should be sure that investigators and IBCs at all involved institutions are appropriately consulted.

R. L. Kirschstein
Ruth L. Kirschstein, M.D.
Committee Chairman

Bernard Talbot
Bernard Talbot, M.D., Ph.D.
Committee Executive Secretary

Figure One


PRV(BUK)
Step 1
Plaque purification
PRV(BUK-5)
BrdUrd treatment
araT treatment
PRV(BUK-5A) TK⁻
recombinant plasmid (a)
pBB11
Step 2
transfection of DNAs and recombination
PRV(BUK-5A-R1) TK⁺
recombinant plasmid (b)
pBB11 dlP4
Step 3
transfection of DNA and recombination
PRV(BUK-dl3) TK⁻

LEGEND FOR FIGURE ONE

Recombinant Plasmids

(a). Plasmid pBB11 was a recombinant plasmid which was a pBR322 derivative containing a 3.5 kilobase insert of the BamHI-11 fragment of TK^+ PRV(BUK).

(b). Plasmid pBB11 dlP4 was a derivative of pBB11, with a deletion of about 148 base pairs in the coding region of the TK gene.

Procedural Steps

1. Pseudorabies Bucharest, [PRV(BUK)], was plaque purified and clone 5, [PRV(BUK-5)], was selected for futher evaluation. The TK^- mutant, PRV(BUK-5A), was derived from the TK^+ PRV (BUK-5) by propagating PRV(BUK-5) in growth media containing gradually increasing concentrations of BrdUrd and araT.

2. Transfecting RAB-9 cells with PRV(BUK-5A) DNA, plus plasmid pBB11, yielded the TK^+ recombinant, PRV(BUK-5A-R1).

3. Transfecting RAB-9 cells with PRV(BUK-5A-R1) DNA, plus plasmid pBB11 dlP4 yielded the TK^- recombinant, PRV(BUK-dl3), which was the final vaccine product which was subsequently tested in pigs.

(Information obtained from Document IV-A)

Attachment A, page 1

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health

Memorandum

Date MAY 7 1986

From Director, NIH

Subject Allegation of Violation of NIH Guidelines for Research Involving Recombinant DNA Molecules

To See Below

Thank you for agreeing to serve on the committee I have just established to review the allegations of violations of the National Institutes of Health Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines) in the conduct of field tests of a pseudorabies vaccine at Baylor College of Medicine and/or Texas A & M University. I am asking you to review the allegations, gather more information as you require, and report to me whether you judge a violation of the NIH Guidelines took place and, if so, what action you recommend NIH should take. Dr. Talbot, Executive Secretary, will be in touch with you to set up the first meeting of the committee. A roster of the membership is attached.

James B. Wyngaarden

James B. Wyngaarden, M.D.

Attachment

Addressees:
Dr. Ruth Kirschstein
✓Dr. Bernard Talbot
Dr. Vida Beaven
Dr. William Gartland
Dr. Susan Gottesman
Mr. Robert Lanman
Dr. Malcolm Martin
Ms. Mary Miers
Dr. Sue Tolin

Attachment A, page 2

Committee to Review Allegations of Violations of the NIH Guidelines for Research Involving Recombinant DNA Molecules in the Conduct of Field Tests of a Pseudorabies Vaccine at Baylor College of Medicine and/or Texas A & M University

Dr. Ruth Kirschstein - Chairman
Director
National Institute of General Medical Sciences, NIH

Dr. Bernard Talbot - Executive Secretary
Deputy Director
National Institute of Allergy and Infectious Diseases, NIH

Dr. Vida Beaven
Special Assistant to the Deputy Director, NIH

Dr. William Gartland
Director
Office of Recombinant DNA Activities
National Institute of Allergy and Infectious Diseases, NIH

Dr. Susan Gottesman
Senior Investigator
Laboratory of Molecular Biology
National Cancer Institute, NIH

Mr. Robert Lanman
NIH Legal Advisor
Office of the General Counsel, HHS

Dr. Malcolm Martin
Chief
Laboratory of Molecular Microbiology
National Institute of Allergy and Infectious Diseases, NIH

Ms. Mary Miers
Institutional Liaison Officer
Office of Extramural Research and Training, NIH

Dr. Sue Tolin
Science & Education Administration
Cooperative State Research Service
Department of Agriculture

Attachment B
Individuals to Whom a Draft of this Report was Sent for Comment

I-Authors of the Scientific Paper (Document IV-B) which Described the Maddox Farm Field Test

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Novagene
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Dr. Stewart McConnell
Professor Emeritus
1610 Dominik Drive
College Station, Texas 77840

II-Chairman, Subcommittee on Recombinant DNA, Biohazard Safety Committee, Baylor College of Medicine

Dr. Alan J. Garber
Chief, Diabetes Metabolism Unit
The Methodist Hospital
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6565 Fannin
Houston, Texas 77030

III-Chairman, Institutional Biosafety Committee, Texas A & M University

Dr. James R. Wild
Professor, Department of Biochemistry & Biophysics
Texas A & M University
College Station, Texas 77843-2128

Attachment B, page 2

IV-Other Officials at Baylor College of Medicine

Dr. William T. Butler
President
Baylor College of Medicine
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Houston, Texas 77030

Dr. Vernon Knight
Chairman, Department of Microbiology and Immunology
Baylor College of Medicine
One Baylor Plaza
Houston, Texas 77030

V-Other Official at Texas A & M University

Dr. Gordon T. Eaton
Provost and Vice President for Academic Affairs
Texas A & M University
College Station, Texas 77843-1248

APPENDIX 10

[REQUEST FOR CLARIFICATION BY MARGARET MELLON, ELI]

Could you please insert the following identifying information in the first paragraph of my statement on page 65 at line 155? I omitted it from my oral statement in the interest of time.

I was trained as a scientist and have done post-doctoral work in molecular virology. I am also an attorney who has practiced environmental law. I am very pleased to have this opportunity to comment on the recently released Coordinated Framework for the Regulation of Biotechnology. The Environmental Law Institute is a nonprofit, non-partisan research and educational organization dedicated to the improvement of environmental law and policy. ELI regards biotechnology as a powerful force that in the coming decades will be major influence on global social, environmental and economic developments. It views the next few years as a golden, but fast-evaporating, opportunity to put in place a reasonable apparatus to evaluate and respond to the technology.

○